```
  pathway.
? s (cd40) and (ctla4? or ctla(w)4?) and (graft? or transplant?)
>>>File 5 processing for 4? stopped at 4D519
>>>File 73 processing for 4? stopped at 4FLD
>>>File 155 processing for 4? stopped at 4LD5
>>>File 399 processing for 4? stopped at 4HOT
          32077  CD40
           5473  CTLA4?
           8479  CTLA
        7765135  4?
           8092  CTLA(W)4?
         695142  GRAFT?
        1825070  TRANSPLANT?
     S21     610  (CD40) AND (CTLA4? OR CTLA(W)4?) AND (GRAFT? OR
                  TRANSPLANT?)
? rd s21
     S22     428  RD S21  (unique items)
? s s22 and py=1990
           428  S22
        1840335  PY=1990
     S23       0  S22 AND PY=1990
? s s22 and py=1991
           428  S22
        1830981  PY=1991
     S24       0  S22 AND PY=1991
? s s22 and py=1992
           428  S22
        1866459  PY=1992
     S25       0  S22 AND PY=1992
? s s22 and py=1993
           428  S22
        1877067  PY=1993
     S26       2  S22 AND PY=1993
? rd s26
     S27       2  RD S26  (unique items)
? t s27/7/all

 27/7/1     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2007 Elsevier B.V. All rts. reserv.

05585673     EMBASE No: 1993353773
  Ligation of B7 with CD28/CTLA-4 on T cells results in CD40 ligand
expression, interleukin-4 secretion and efficient help for antibody
production by B cells
  De Boer M.; Kasran A.; Kwekkeboom J.; Walter H.; Vandenberghe P.;
Ceuppens J.L.
  Department of Immunology, Innogenetics NV, Industriepark Zwijnaarde
  7,B-9052 Ghent  Belgium
  European Journal of Immunology ( EUR. J. IMMUNOL. ) (Germany)  1993,
  23/12 (3120-3125)
  CODEN: EJIMA   ISSN: 0014-2980
  DOCUMENT TYPE: Journal; Article
  LANGUAGE: ENGLISH   SUMMARY LANGUAGE: ENGLISH

  It has been extensively shown that when T cells are co-stimulated with
B7-CD28 interaction, a strong proliferative as well as cytolytic T cell
response can be induced. In contrast, there exists only indirect evidence
that the B7-CD28 interaction is of importance for the induction of T cell
helper functions in B cell responses. Here we have used mouse fibroblasts
transfected with the human Fcgamma receptor type II and human B7 to address
this issue. We found that T cells, when activated through the T cell
receptor (TcR)/CD3 complex with monoclonal antibodies and co-stimulated by
B7-CD28 interaction, can provide efficient help for the induction of both
```

IgM and IgG production by resting B cells. This helper activity is, at least in part, mediated by the interaction between the CD40 ligand on the T cells and CD40 on the B cells. We also demonstrate that more than one signal to the T cell is required for the induction of the CD40 ligand, one being delivered through the TcR/CD3 complex and the second by ligation of CD28 with the B7 molecule. In addition to the induction of cognate T helper function, we provide evidence that co-stimulation of T cells with B7-CD28 interaction can result in the secretion of both Th1- and Th2-type lymphokines.

27/7/2 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

05329297 EMBASE No: 1993097382
Activated T cells induce expression of B7/BB1 on normal or leukemic B cells through a CD40-dependent signal
Ranheim E.A.; Kipps T.J.
University of California, 9500 Gilman Drive,San Diego, CA 92093-0663 United States
Journal of Experimental Medicine (J. EXP. MED.) (United States) 1993, 177/4 (925-935)
CODEN: JEMEA ISSN: 0022-1007
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Cognate interactions between antigen-presenting B and T cells play crucial roles in immunologic responses. T cells that have been activated via the crosslinking of CD3 are able to induce B cell proliferation and immunoglobulin secretion in a major histocompatibility complex-unrestricted and contact-dependent manner. We find that such activated human CD4sup + T cells, but not control Ig-treated T cells, may induce normal or leukemic B cells to express B7/BB1 and significantly higher levels of CD54 intercellular adhesion molecule 1 via a process that also requires direct cell-cell contact. To discern what cell surface molecule(s) may be responsible for signalling B cells to express B7/BB1, we added various monoclonal antibodies (mAbs) specific for T or B cell accessory molecules or control mAbs to cocultures of alpha-CD3-activated T cells and resting B cells. We find that only alpha- ***CD40*** mAbs can significantly inhibit the increased expression of B7/BB1, suggesting that the ligand for CD40 expressed on activated T cells may be an important inducer of B7/BB1 expression. Subsequent experiments in fact demonstrate that alpha-CD40 mAbs, but not control mAbs, induce changes in B cell phenotype similar to those induced by activated T cells when the mAbs are presented on FcgammaRII (CDw32)-expressing L cells. These phenotypic changes have significant effects on B cell function. Whereas chronic lymphocytic leukemia (CLL) B cells normally are very poor stimulators in allogeneic mixed lymphocyte reactions (MLRs), CLL-B cells preactivated via CD40 crosslinking are significantly better presenters of alloantigen, affecting up to 30-fold- greater stimulation of T cell proliferation than that induced by control treated or nontreated CLL-B cells. Similarly, the MLR of T cells stimulated by allogeneic nonleukemic B cells can be enhanced significantly if the stimulator B cells are preactivated via CD40 crosslinking. The enhanced MLR generated by such preactivated B cells may be inhibited by blocking B7/BB1- CD28 interaction with ***CTLA4Ig*** . These studies demonstrate a novel, CD40- dependent pathway for inducing B cell expression of B7/BB1 and enhancing B cell antigen-presenting cell activity that can be initiated via cell-cell contact with alpha-CD3-stimulated CD4sup + T cells.

? s s22 and py=1994
428 S22
1932880 PY=1994
S28 5 S22 AND PY=1994

? t s28/7/all

28/7/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05919169 EMBASE No: 1994332300
The tissue distribution of the B7-2 costimulator in mice: Abundant expression on dendritic cells in situ and during maturation in vitro
Inaba K.; Witmer-Pack M.; Inaba M.; Hathcock K.S.; Sakuta H.; Azuma M.; Yagita H.; Okumura K.; Linsley P.S.; Ikehara S.; Muramatsu S.; Hodes R.J.; Steinman R.M.
Cellular Physiology/Immunology Laboratory, Rockefeller University, Box 176, 1230 York Avenue,New York, NY 10021 United States
Journal of Experimental Medicine (J. EXP. MED.) (United States) 1994, 180/5 (1849-1860)
CODEN: JEMEA ISSN: 0022-1007
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

B7-2 is a recently discovered, second ligand for the CTLA-4 /CD28, T cell signaling system. Using the GL-1 rat monoclonal antibody (mAb), we monitored expression of B7-2 on mouse leukocytes with an emphasis on dendritic cells. By cytofluorography, little or no B7-2 was detected on most cell types isolated from spleen, thymus, peritoneal cavity, skin, marrow, and blood. However, expression of B7-2 could be upregulated in culture. In the case of epidermal and spleen dendritic cells, which become highly immunostimulatory for T cells during a short period of culture, the upregulation of B7-2 was dramatic and did not require added stimuli. Lipopolysaccharide did not upregulate B7-2 levels on dendritic cells, in contrast to macrophages and B cells. By indirect immunolabeling, the level of staining with GL-1 mAb exceeded that seen with rat mAbs to several other surface molecules including intercellular adhesion molecule 1, B7-1, CD44, and CD45, as well as new hamster mAbs to ***CD40*** , CD48, and B7-1/CD80. Of these accessory molecules, B7- 2 was a major species that increased in culture, implying a key role for B7- 2 in the functional maturation of dendritic cells. B7-2 was the main (>90%) ***CTLA*** - ***4*** ligand on mouse dendritic cells. When we applied GL-1 to tissue sections of a dozen different organs, clear-cut staining with B7-2 antigen was found in many. B7-2 staining was noted on liver Kupffer cells, interstitial cells of heart and lung, and profiles in the submucosa of the esophagus. B7-2 staining was minimal in the kidney and in the nonlymphoid regions of the gut, and was not observed at all in the brain. In the tongue, only rare dendritic cells in the oral epithelium were B7-2sup +, but reactive cells were scattered about the interstitial spaces of the muscle. In all lymphoid tissues, Gl-1 strongly stained certain distinct regions that are occupied by dendritic cells and by macrophages. For dendritic cells, these include the thymic medulla, splenic periarterial sheaths, and lymph node deep cortex; for macrophages, the B7-2-rich regions included the splenic marginal zone and lymph node subcapsular cortex. Splenic B7-2sup + cells were accessible to labeling with GL-1 mAb given intravenously. Dendritic cell stimulation of T cells (DNA synthesis) during the mixed leukocyte reaction was significantly (35-65%) blocked by GL-1. The block could be enhanced by adding 1G10 anti-B7-1 or by using ***CTLA*** - ***4*** Ig, a ligand for both B7-1 and B7-2. We conclude that B7-2, like other accessory molecules, is expressed by many types of antigen- presenting cells. However, the regulation and extent of B7-2 expression seems to differ among cell types. Dendritic cells express very high levels, in several sites in vivo and after maturation into strong accessory cells in culture.

28/7/2 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

05823482 EMBASE No: 1994199748
The B7 and CD28 receptor families
June C.H.; Bluestone J.A.; Nadler L.M.; Thompson C.B.
Department of Medicine, Uniformed Services University, Health Sciences,Bethesda, MD 20889 United States
Immunology Today (IMMUNOL. TODAY) (United Kingdom) 1994, 15/7 (321-331)
CODEN: IMTOD ISSN: 0167-5699
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Current evidence suggests that T-cell receptor (TCR) recognition of antigen bound to the major histocompatibility complex (Ag-MHC) is insufficient to lead to T-cell proliferation or effector function. For a helper T cell to produce sufficient interleukin 2 (IL-2) to allow autocrine-driven clonal expansion, there is a requirement for so-called 'co-stimulatory' or 'accessory' signals in addition to TCR ligation by Ag-MHC. The interaction of the CD28 receptor on T cells with B7 on antigen-presenting cells (APCs) supplies one such co-stimulatory signal. However, the recent discovery that CD28 and B7 are each members of larger gene families suggests that the regulation of co-stimulation is more complex than previously imagined. Here, Carl June and colleagues highlight recent advances in the understanding of the CD28 and B7 receptor families.

28/7/3 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

05670734 EMBASE No: 1994087113
Helper effector function of human T cells stimulated by anti-CD3 mAb can be enhanced by co-stimulatory signals and is partially dependent on CD40-CD40 ligand interaction
Kwekkeboom J.; De Rijk D.; Kasran A.; Barcy S.; De Groot C.; De Boer M.
Laboratory Cell Biology Histology, University of Amsterdam, Academic Medical Center, Meibergdreef 15,NL-1105 AZ Amsterdam Netherlands
European Journal of Immunology (EUR. J. IMMUNOL.) (Germany) 1994, 24/3 (508-517)
CODEN: EJIMA ISSN: 0014-2980
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

In this study we have investigated whether anti-CD3-induced human T cell help for immunoglobulin production could be enhanced by co-stimulation of the T cells via other T cell surface molecules, and the contribution of CD40-CD40 ligand interaction to the execution of T helper effector function induced by these different stimulatory signals. In a system in which irradiated tonsillar T cells were stimulated with immobilized anti-CD3 monoclonal antibody (mAb) , it was found that ligation of CD2 with a mitogenic pair of mAb considerably enhanced anti-CD3-induced T cell help for immunoglobulin production. Likewise, ligation of CD28 with mAb enhanced T helper activity, although to a lesser extent. Upon addition of anti-CD28 and anti-CD2 mAb together, an even higher immunoglobulin production was observed. This combination resulted in a four- to fivefold increase in immunoglobulin production as compared to cultures in which T cells were stimulated with anti-CD3 mAb alone. The effect of ligation with B7, the natural ligand of CD28, was studied in a system which utilizes the presentation of anti-CD3 mAb on human FcgammaRII-expressing mouse fibroblasts which were co-transfected with human B7. It appeared that B7 could stimulate help for immunoglobulin production much more efficiently than ligation of CD28 with mAb did. Physical separation of B cells from T cells led to complete abrogation of immunoglobulin production. Blocking of CD40 with specific mAb, which have no intrinsic B cell stimulatory

properties, or the CD40 ligand with a soluble CD40-human IgM fusion protein, resulted in dose-dependent, but only partial, inhibition of T cell-dependent immunoglobulin production with all modes of T cell activation tested. A clear correlation was found between the induction of CD40 ligand expression on the T cells by the different modes of co-stimulation and subsequent immunoglobulin production by the B cells. It is concluded that ligation of CD28 and/or CTLA-4, and of CD2 can generate co-stimulatory signals for T cell help for immunoglobulin production, which was found to be only partially dependent on the ***CD40*** - ***CD40*** ligand interaction.

28/7/4 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

05641415 EMBASE No: 1994047566
Signals and signs for lymphocyte responses
Janeway Jr. C.A.; Bottomly K.
Section of Immunobiology, Howard Hughes Medical Institute, Yale University School of Medicine,New Haven, CT 06510 United States
Cell (CELL) (United States) 1994, 76/2 (275-285)
CODEN: CELLB ISSN: 0092-8674
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The adaptive immune response protects us from infection in a world of pathogens that is forever evolving new variants. As the system is built on the generation of an open repertoire of receptors, the recognition of self is unavoidable, and is guarded against by deletion during lymphocyte development of those cells that are specific for ubiquitous self antigens, and the silencing of those that are specific for self antigens only encountered after cells achieve functional maturity in the periphery. This silencing occurs when lymphocytes recognize antigens in the absence of suitable costimulatory molecules. By contrast, when the same cell encounters the same ligand on a cell that expresses costimulatory molecules, it will proliferate and differentiate into an effector cell. These effector cells mediate protective immunity when the antigen is carried by a pathogen, but they can mount autoimmune responses if the antigen is derived from self. The major costimulatory molecules for CD4 T cells appear to be B7 and B7.2 that bind to the CD28 and ***CTLA*** - ***4*** receptors on the T cell. The signals from the TCR appear to be integrated with those from the costimulator receptor, and the T cell response depends on the precise nature of these signals, further conditioned by cytokines present in the environment of the responding cell. B cells can be viewed in a similar way, with the costimulatory molecule CD40 ligand and cytokines coming mainly from CD4 helper T cells determining the fate of the responding B cell. The TCR is not simply an on and off switch, since the precise way in which the TCR is ligated determines the differentiation of the T cell and can alter the effector responses of established T cell lines. Thus, the response capabilities of T cells are more flexible than originally believed, and much of this flexibility comes from the interplay of TCR signals and signs from the environment. If the biochemical nature of these differential signaling pathways were known, it might be possible to develop simple pharmacological agents capable of diverting T cell responses from harmful to innocuous by getting the T cell to reinterpret the signals it is receiving via its receptors. This approach to immunomodulation could be generic, using the antigens already perturbing the system to select the T cells one wishes to affect with the drug. Understanding the biochemical signaling pathways leading from receptor and costimulator to response may allow such agents to be identified by intention.

28/7/5 (Item 5 from file: 73)

DIALOG(R)File 73:EMBASE

05609955 EMBASE No: 1994024192
Induction of B cell costimulatory function by recombinant murine CD40 ligand
Kennedy M.K.; Mohler K.M.; Shanebeck K.D.; Baum P.R.; Picha K.S.; Otten-Evans C.A.; Janeway Jr. C.A.; Grabstein K.H.
Department of Immunobiology, Immunex Research and Dev Corporation, 51 University Street,Seattle, WA 98101 United States
European Journal of Immunology (EUR. J. IMMUNOL.) (Germany) 1994, 24/1 (116-123)
CODEN: EJIMA ISSN: 0014-2980
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

T cell-dependent regulation of B cell growth and differentiation involves an interaction between CD40, a B cell surface molecule, and the ***CD40*** ligand (CD40L) which is expressed on activated CD4sup + T cells. In the current study, we show that recombinant membrane-bound murine CD40L induces B cells to express costimulatory function for the proliferation of CD4sup + T cells. CD40L- or lipopolysaccharide (LPS)-activated, but not control-cultured B cells were strong costimulators of anti-CD3 or alloantigen-dependent T cell responses. The molecular interactions responsible for the increased costimulatory functions were examined by analyzing the activated B cells for changes in the expression of two costimulatory molecules, B7 and heat-stable antigen (HSA), as well as by the use of antagonists of B7 and HSA (***CTLA4*** .Fc and 20C9, respectively). The expression of both B7 and HSA was enhanced on B cells activated with LPS. As observed in previous studies, the costimulatory activity of the LPS-activated B cells was dependent on both B7 and HSA and was completely inhibited in the presence of a combination of ***CTLA4*** .Fc and 20C9. In contrast, activation of B cells with CD40L induced the expression of B7 but did not enhance the expression of HSA. In addition the costimulatory activity of the CD40L-activated B cells was partially, but not completely, inhibited by the combination of ***CTLA4*** .Fc and 20C9. These results demonstrate that CD40L regulates costimulatory function of B cells in part by inducing the expression of B7 and suggest that CD40L-activated B cells express an additional costimulatory activity that is not associated with LPS-activated B cells.

```
? s s22 and py=1995
             428  S22
         1982323  PY=1995
     S29       9  S22 AND PY=1995
? t s29/7/all
```

29/7/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

06305764 EMBASE No: 1995343976
Localization in situ of the co-stimulatory molecules B7.1, B7.2, CD40 and their ligands in normal human lymphoid tissue
Vyth-Dreese F.A.; Dellemijn T.A.M.; Majoor D.; De Jong D.
Division of Immunology, The Netherlands Cancer Institute, Plesmanlaan 121,1066 CX Amsterdam Netherlands
European Journal of Immunology (EUR. J. IMMUNOL.) (Germany) 1995, 25/11 (3023-3029)
CODEN: EJIMA ISSN: 0014-2980
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Functional interactions between B and T lymphocytes are known to depend on the expression of co-stimulatory molecules B7.1/CD80, B7.2/CD86 and

their counter-receptors CD28 and CTLA4, as well as CD40 and its ligand CD40L. To study the role of these molecules in situ, an immunohistochemical analysis was carried out on normal human lymphoid tissue. In the germinal centers (GC), B7.1 and B7.2 were differentially expressed. In the dark zone, centroblasts were predominantly B7.1sup +, while centrocytes in the light zone were B7.2sup +, resulting in reversed gradients of both markers in GC. Follicle mantle cells were negative for B7.1 and B7.2. Macrophages and interdigitating dendritic cells (IDC) in T cell zones both expressed B7.1 and B7.2. Moreover, clusters of B7.2sup + T cells were demonstrated in interfollicular areas. Intrafollicular CD4sup + T cells in GC, predominantly in the apical light zone, expressed CD28 and ***CTLA4*** , as did the majority of interfollicular T cells. ***CTLA4*** showed a striking excentric cytoplasmic staining, which was also seen on T cells activated in vitro. ***CD40*** was expressed on all B cells and more strongly on macrophages and IDC. Moreover, small clusters of T cells in a rim outside the GC showed ***CD40*** expression. CD40L was expressed both on intrafollicular CD4sup + T cells as well as on T cells in T cell zones. The differential distribution of co-stimulatory molecules in different compartments of normal human lymphoid,tissue in situ indicates that these interactions play a distinctive role in different stages of B cell differentiation and in the immune response.

29/7/2 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

06299157 EMBASE No: 1995338152
A T cell lymphoma can provide potent co-stimulatory effects to T cells that are not mediated by B7-1, B7-2, CD40, HSA or CD70
Nieland J.D.; Kruisbeek A.M.
Division of Immunology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Huis, Plesmanlaan 121,1066 CX Amsterdam Netherlands
International Immunology (INT. IMMUNOL.) (United Kingdom) 1995, 7/11 (1827-1838)
CODEN: INIME ISSN: 0953-8178
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Dominant second signals for T cell activation can be generated through interactions between CD28 and CTLA-4 on T cells with their co-stimulatory ligands B7-1 and B7-2 on APC. Nevertheless, some B7-negative cell lines appear capable of providing second signals to T cells, illustrating that B7-independent co-stimulatory pathways may exist. One such cell line, the peptide-transporter defective T lymphoma RMA-S, was investigated in the present study, to determine the origin of the co-stimulatory effects it provides. RMA-S can support clonal expansion of purified CD4 or CD8 T cells from unprimed mice activated with concanavalin A (ConA) or immobilized anti-CD3. Nevertheless, RMA-S does not express B7-1 or B7-2, nor does it express other known co-stimulatory molecules, i.e. ***CD40*** , gp39, CD70 and HSA. Also, co-stimulation provided by RMA-S could not be blocked by antibodies or fusion proteins specific for these co-stimulatory molecules, excluding their participation. However, RMA-S' co-stimulatory activity is dependent on adhesive interactions. RMA-S is incapable of IL-2 production in the presence of ConA or anti-CD3, but T cells co-stimulated by RMA-S produce IL-2 and IFN-gamma upon anti-CD3- or ConA-induced activation. Furthermore, co-stimulation of antigen-specific T cell proliferation of both class I- and class II-restricted T cell clones can be provided by RMA-S, and RMA-S can preclude induction of anergy by 1-ethyl-3-(3-dimethyl amino propyl)carboiimide-fixed APC in a class II-restricted T cell clone. The results suggest that potent co-stimulatory pathways can be induced by cellular interactions between a T lymphoma, RMA-S and T cells, not involving gp39, CD40, CD70, HSA, B7-1 (CD80) or B7-2 (CD86). Characterization of the molecules involved is in progress.

29/7/3 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

06254035 EMBASE No: 1995280135
Influence of MHC class I molecules on T-cell proliferation induced by CD3 or Thy-1 stimulation
Amirayan N.; Furrie Deleuil E.F.; Mellor A.; Leserman L.; Machy P.
Centre d'Immunology, INSERM-CNRS de Marseille-Luminy,13288 Marseille Cedex 9 France
Immunology (IMMUNOLOGY) (United Kingdom) 1995, 86/1 (71-78)
CODEN: IMMUA ISSN: 0019-2805
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We have reported that class I- (and lymphocyte function-associated antigen-1 (LFA-1-)) specific monoclonal antibodies (mAb) inhibit anti-CD3-mediated activation of naive T cells. The present study investigated the mechanism of this inhibition. CD28-specific mAb augmented stimulation induced by soluble CD3 mAb, but this costimulation was also inhibited by anti-class I or anti-LFA-1 mAb. However, stimulation of T cells was not inhibited when activated B cells were present. Neither B7-1- nor B7-2-specific blocking mAb or soluble CTLA-4, CD40 or gp39 restored the inhibition. Thus, other molecules expressed on activated B cells are implicated far T-cell activation, which could compensate blockade of class I or LFA-1 molecules. Inhibition induced by class I-specific mAb could potentially be mediated through extracellular, transmembrane or cytoplasmic domains of the target molecules. These possibilities were evaluated by the use of mice transgenic for the Qa-2 molecule, selected for expression of Qa-2 at levels equivalent to classical class I molecules. Qa-2 is inserted in the membrane through phosphatidylinositol linkages. Antibodies directed to Qa-2 inhibited CD3-induced stimulation, demonstrating that cytoplasmic and transmembrane protein sequences of class I molecules are not necessary for the inhibitory effect. Inhibition thus presumably depends on extracellular domains. Finally, T cells from betainf 2- microglobulin knock-out mice responded to CD3-specific mAb as well as their class I-positive littermates. Nevertheless, stimulation of T cells from these mice with mitogenic anti-Thy-1 mAb was markedly reduced. Signalling by Thy-1 and the CD3 complex may normally occur through pathways in which class I molecules are implicated.

29/7/4 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06243973 EMBASE No: 1995280659
Induction of CD80 expression in low-grade B cell lymphoma - A potential immunotherapeutic target
Shamash J.; Davies D.C.; Salam A.; Rohatiner A.Z.S.; Young B.D.; Lister T.A.
Department of Medical Oncology, St Bartholomew's Hospital,West Smithfield, London, EC1A 7BE United Kingdom
Leukemia (LEUKEMIA) (United Kingdom) 1995, 9/8 (1349-1352)
CODEN: LEUKE ISSN: 0887-6924
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The CD80 antigen (B7) is expressed on activated B lymphocytes. It is thought to be important in eliciting a T cell response via its ligands CD28 and CTLA-4 when antigen is presented in the presence of the

MHC-1 peptide. Low-grade B cell lymphomas analysed by flow cytometry express CD80 very poorly. However, when grown in vitro using the IL-4/anti-CD40 stromal cell culture system, following depletion of T and IgD-bearing cells, a monoclonal B cell expansion occurs. Cells harvested at days 10-13 express the antigen strongly, regardless of the histological subtype of lymphoma. Further investigation of CD80-mediated immune functions may be possible using this system as a basis for testing immunotherapy.

29/7/5 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

06218456 EMBASE No: 1995247346
Activated T cells can induce high levels of CTLA-4 expression on B cells
Kuiper H.M.; Brouwer M.; Linsley P.S.; Van Lier R.A.W.
Central Laboratory of NRCBTS, Clinical Viro-Immunology Department, Plesmanlaan 125,1066 CX Amsterdam Netherlands
Journal of Immunology (J. IMMUNOL.) (United States) 1995, 155/4 (1776-1783)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Engagement of the TCR/CD3 complex together with ligation of CD28 by its counterstructures B7-1 (CD80) and B7-2 (CD86) on APC are required for mitogenic T cell activation. After activation, T cells not only express B7-1 and B7-2 molecules, but a second receptor for the B7 ligands, ***CTLA*** - ***4*** , can be found on their surfaces. We here show that B cells can be induced to express ***CTLA*** - ***4*** on the plasma membrane. Similar to what has been reported for T cells, CTLA-4 expression on B cells was transient. Purified B cells did not express CTLA-4 when mitogenically activated with alphalgM and CD40 Ab, but did express the molecule when cultured in the presence of membranes from activated T cells, which suggests that induction of CTLA-4 expression on B cells was dependent on direct cell-cell contact of B lymphocytes and activated T cells. ***CTLA*** - ***4*** molecules isolated from either T or B cells were biochemically indistinguishable. Moreover, because the ability of chimeric B7-1/Ig proteins to bind to activated B cells was correlated with CTLA-4 expression levels on these cells, we conclude that B cell-expressed ***CTLA*** - ***4*** has ligand binding capacity. These data suggest that costimulatory receptors and their specific ligands not only play a role in T cell stimulation, but contribute in a direct fashion to the regulation of B cell responses.

29/7/6 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

06171396 EMBASE No: 1995208460
Cellular interaction in germinal centers: Roles of CD40 ligand and B7-2 in established germinal centers
Han S.; Hathcock K.; Zheng B.; Kepler T.B.; Hodes R.; Kelsoe G.
Microbiology/Immunology Department, University of Maryland School of Medicine, 655 West Baltimore Street,Baltimore, MD 21201 United States
Journal of Immunology (J. IMMUNOL.) (United States) 1995, 155/2 (556-567)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Costimulatory interactions between T and B lymphocytes are crucial for T cell activation and B cell proliferation and differentiation. We have compared the roles of CD40L and B7-2 in the initiation and maturation of humoral immunity by administering anti-CD40 ligand (L) or anti-B7-2 Ab during the early (days - 1 to 3) or late (days 6-10) phases of primary responses to thymus-dependent (Td) and -independent (Ti) Ags. Germinal center (GC) formation in response to a Td Ag was inhibited completely by the early administration of anti-CD40L or anti-B7-2 Absolute Later in the response, established GCs remained sensitive to anti-CD40L but were resistant to treatment with anti-B7-2. However, Ig hypermutation was reduced dramatically in GCs of anti-B7-2-treated mice and humoral memory was impaired. Early administration of anti-CD40L reduced serum Ab levels to ~10% of controls, whereas early treatment with anti-B7-2 reduced Ab production by only 50%. Later treatments with either Ab had no effect on Ab production. Response to a type II Ti Ag was more resistant than Td responses to interruption of costimulatory interactions. Our findings suggest that the costimulatory roles of CD40:CD40L and B7-2:CD28/ CTLA-4 differ in the GC; administration of anti- CD40L abrogates an established GC reaction, whereas Ab to B7-2 suppresses Ig hypermutation and entry into the B cell memory compartment. Once B cells have entered the differentiation pathway to Ab production, neither CD40L nor B7-2 is necessary for their continued differentiation and persistence.

29/7/7 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

06137317 EMBASE No: 1995172852
Antibody production: Regulation by cytokines and T-B interactions
SIGNAUX DE LA COOPERATION T-B ET PRODUCTION D'ANTICORPS
Richard Y.; Galanaud P.
Inserm U 131, Institut Paris Sud sur les cytokines, 32 rue des Carnets,92140 Clamart France
Medecine/Sciences (MED. SCI.) (France) 1995, 11/5 (691-702)
CODEN: MSMSE ISSN: 0767-0974
DOCUMENT TYPE: Journal; Review
LANGUAGE: FRENCH SUMMARY LANGUAGE: FRENCH; ENGLISH

In response to antigenic stimulation, B lymphocytes differentiate into antibody producing cells or into memory cells. The specific B cell receptor (BCR) is composed of membrane immunoglobulin (Ig), acting as a ligand subunit, and of invariant heterodimer (alpha/beta) required for stable membrane BCR as well as for interaction with cytoplasmic signalling molecules. alpha and beta chains, linked to different proximal effector enzymes (Src-PTK, PTK 72 and PI3K), deliver synergistic activation signals to the B cells. Co-receptor molecules (CD19/CD21 complex and CD22 molecule) amplify the antigenic signal and may prevent low efficiency triggering through the BCR. Antigen-induced BCR stimulation results in the expression of new surface molecules, the production of cytokines and the capacity to present antigen fragments bound to the MHC class II. To progress in their differentiation process, additional signals must be provided to activated B cells through direct T-B interactions and by cytokines secreted by activated T cells. The former involves integrin and selectins but also more specific ligand sets such as CD40/CD40-L and B7/CD28/ ***CTLA*** - ***4*** respectively. The ***CD40*** / ***CD40*** -L complex plays a key role in B cell switching and in the selection process leading to high affinity anti-body producing cells. In contrast, B7CD28/ ***CTLA*** - ***4*** interactions seem essential to fully achieve T cell activation and interleukin-dependent T cell expansion. An efficient humoral response also requires the secretion of Th-2 cytokines by activated CD4 T cells. These cytokines act at different levels of the B cell maturation in sustaining

early B cell activation (IL4, IL13), isotype switching (IL4, IL5, IL13) or plasma cell differentiation (IL6, IL10). In this issue, we focus our attention on some crucial events of the B cell differentiation: (1) BCR signalling, (2) critical pairs of molecules involved on B-T interactions and (3) cytokines produced in the vicinity of B cells.

29/7/8 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

06121745 EMBASE No: 1995152539
Basic aspects of neuroimmunology as they relate to immunotherapeutic targets: Present and future prospects
Dalakas M.C.
Medical Neurology Branch, NINDS, NIH, 10 Center Drive,Bethesda, MD 20892-1382 United States
Annals of Neurology (ANN. NEUROL.) (United States) 1995, 37/SUPPL. 1 (S2-S13)
CODEN: ANNED ISSN: 0364-5134
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The neurological diseases with definite or putative immune pathogenesis include myasthenia gravis; Lambert-Eaton myasthenic syndrome; IgM monoclonal anti-myelin-associated glycoprotein-associated demyelinating polyneuropathy; Guillain-Barre syndrome; chronic inflammatory demyelinating polyneuropathy; multifocal motor neuropathy with or without GMinf 1 antibodies; multiple sclerosis; inflammatory myopathies; stiff-man syndrome; autoimmune neuromyotonia; paraneoplastic neuronopathies and cerebellar degeneration; and neurological diseases associated with systemic autoimmune conditions, vasculitis, or viral infections. The events that lead to these autoimmune diseases are not clear but the following sequential steps are critical: (a) the breaking of tolerance, a process in which cytokines, molecular mimicry, or superantigens may play a role in rendering previously anergic T cells to recognize neural autoantigens; (b) antigen recognition by the T-cell receptor complex and processing of the antigen via the major histocompatibility complex class I or II; (c) costimulatory factors especially B7 and B7- binding proteins (CD28, CTLA-4) and intercellular adhesion molecule (ICAM)-1 and its leukocyte function-associated (LFA)-1 ligand; (d) traffic of the activated T cells across the blood-brain or blood-nerve barrier via a series of adhesion molecules that include selectins, leukocyte integrins (LFA-1, Mac-1, very late activating antigen (VLA)-4) and their counterreceptors (ICAM-1, vascular cell adhesion molecule (VCAM)) on the endothelial cells; and (e) tissue injury when the activated T cells, macrophages, or specific autoantibodies find their antigenic targets on glial cells, myelin, axon, calcium channels, or muscle. In designing specific immunotherapy, the main players involved in every step of the immune response need to be considered. Targets for specific therapy in neurological diseases include agents that (a) interfere or compete with antigen recognition or stimulation, (b) inhibit costimulatory signals or cytokines, (c) inhibit the traffic of the activated cells to tissues, and (d) intervene at the antigen recognition sites in the targeted organ. The various immunomodulating procedures and immunosuppressive drugs currently used for nonselective neuroimmunotherapy are discussed in the context of their interference with the above-described immune mediators.

29/7/9 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

06058426 EMBASE No: 1995088841

Studies on the interdependence of gp39 and B7 expression and function during antigen-specific immune responses

Roy M.; Aruffo A.; Ledbetter J.; Linsley P.; Kehry H.; Noelle R.
Department of Microbiology, Dartmouth Medical School, 1 Medical Center Drive,Lebanon, NH 03756 United States

European Journal of Immunology (EUR. J. IMMUNOL.) (Germany) 1995, 25/2 (596-603)
CODEN: EJIMA ISSN: 0014-2980
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Interactions between T and B cells are dynamic and regulated by interacting receptor: co-receptors. Interactions between ***CD40*** and its ligand, gp39, and the CD28/CTLA-4 and B7 family members play a decisive role in regulating tile progression of cognate interactions. The interdependence of gp39-CD30 and CD28/CTLA-B7 expression and function was studied in vitro during all antigen-induced immune response using T cells from mice expressing a transgenic T cell receptor (TCR). gp39 was induced on pigeon cytochrome c (PCC)-transgenic T cells in the presence of antigen and antigen-presenting cells, The antigen-induced expression of gp39 on transgenic T cells was inhibited by antibodies to class II major histocompatibility complex, CD4 and LFA-1, but not by CTLA-4 Ig, anti-B7-1 or anti-B7-2. These data established that The antigen-induced expression of gp39 was not dependent on co-stimulation via CD28/CTLA-***4*** . The addition of PCC also resulted in the modest expression of B7-1 and a more robust expression of B7-2 on the cognate B cells. The addition of anti-gp39 blocked the up-regulated expression of B7-1 and partially blocked the up-regulated expression of B7-2. The addition of anti-gp39 and anti-interleukin-4 inhibited antigen-induced expression of B7-2 on B cells to near background levels. Studies on the up-regulation of B7-1 and B7-2 on resting B cells showed that soluble gp39 up-regulated B7-1 and B7-2 expression on B cells, In addition, interleukin-4, and interferon-gamma up-regulated B7-2 expression on B cells. Taken together, these data demonstrate that the antigen-induced expression of gp39 is dependent on TCR-derived signals, yet independent of CD28/CTLA-4 co-stimulatory signals. Cognate interactions also resulted in the modest enhancement: of B7-1 expression and a more profound expression of B7-2 which were completely or partially dependent on gp39-CD40 interactions.

```
? s s22 and py=1996
             428  S22
         2076377  PY=1996
     S30      13  S22 AND PY=1996
? t s30/7/all

 30/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2007 The Thomson Corporation. All rts. reserv.
```

13685297 BIOSIS NO.: 199799319357
Costimulatory function and expression of CD40 ligand, CD80, and CD86 in vascularized murine cardiac allograft rejection

AUTHOR: Hancock Wayne W; Sayegh Mohamed H; Zheng Xiang-Guang; Peach Robert; Linsley Peter S; Turka Laurence A (Reprint)
AUTHOR ADDRESS: Univ. Pennsylvania, 409 BRB-I, 422 Curie Boulevard, Philadelphia, PA 19104-6069, USA**USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 93 (24): p13967-13972 1996 1996
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recent data implicates a role for the CD40-CD40

ligand (CD40L) pathway in ***graft*** rejection. One potential mechanism is direct costimulation of T cells through CD40L. Alternatively, the ability of CD40 stimulation to induce CD80 (B7-1) and CD86 (B7-2) expression on antigen-presenting cells (APCs) has led to the hypothesis that the role of CD40-CD40L interactions in transplant rejection might be indirect, i.e., to promote the costimulatory capacity of APCs. Here, we have used a murine vascularized cardiac allograft model to test this hypothesis. Treatment of the recipients with donor splenocytes and a single dose of anti-CD40L mAb induces long-term ***graft*** survival (gt 100 days) in all animals. This is associated with marked inhibition of intragraft Th1 cytokine (interferon gamma and interleukin (IL) 2) and IL-12 expression with reciprocal up-regulation of Th2 cytokines (IL-4 and IL-10). In untreated allograft recipients, CD86 is strongly expressed on endothelial cells and infiltrating mononuclear cells of the ***graft*** within 24 hr. In contrast, CD80 expression is not seen until 72 hr after engraftment. Anti-CD40L mAb has no detectable effect on CD86 up-regulation, but almost completely abolishes induction of CD80. However, animals treated with anti-CD80 mAb or with a mutated form of CTLA4Ig (which does not bind to CD86) rejected their cardiac allografts, indicating that blockade of CD80 alone does not mediate the ***graft*** -prolonging effects of anti-CD40L mAb. These data support the notion that the role of CD40-CD40L in transplant rejection is not solely to promote CD80 or CD86 expression, but rather that this pathway can directly and independently costimulate T cells. These data also suggest that long-term graft survival can be achieved without blockade of either T cell receptor-mediated signals or CD28-CD86 engagement.

30/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13566431 BIOSIS NO.: 199699200491
Immunomodulation in experimental and clinical nephrology using chimeric proteins
AUTHOR: Kunzendorf Ulrich (Reprint); Pohl Thomas; Bulfone-Paus Silvia; Krause Hans; Ziegler Ekkehard; Onu Adrian; Distler Armin
AUTHOR ADDRESS: Universitaetsklin. Benjamin Franklin, Abteilung Innere Med., Hindenburgdamm 30, D-12200 Berlin, Germany**Germany
JOURNAL: Kidney and Blood Pressure Research 19 (3-4): p201-204 1996
1996
ISSN: 1420-4096
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The objective of immunosuppressive therapy in nephrology is to prevent autoimmune diseases and to suppress kidney allograft rejections while sparing other effects. Increased clarification of the underlying immune mechanism has made specific immunodulation possible using chimeric proteins in which the variable domains of an immunoglobulin are replaced by extracellular domains of cell surface molecules or cytokines. The immunosuppressive effects of fusion proteins such as CTLA-4 IgG, CD40 IgG, interleukin (IL)-10 IgG, IL-2 IgG or tumor necrosis factor (TNF)-receptor IgG have been proven in various animal models. Moreover, the application of TNF-receptor IgG successfully limited the OKT3-induced cytokine release syndrome in kidney ***graft*** recipients. It seems likely that recombinant proteins with increasingly effective suppression of specific elements of the immune response will become an essential element in clinical protocols.

30/7/3 (Item 1 from file: 73)

06728628 EMBASE No: 1997010090
The role of CD40 ligand in costimulation and T-Cell activation
Grewal I.S.; Flavel R.A.
Dr. R.A. Flavel, Howard Hughes Medical Institute, Section of Immunobiology, Yale University School of Medicine, New Haven, CT 06510 United States
Immunological Reviews (IMMUNOL. REV.) (Denmark) 1996, -/153 (85-106)
CODEN: IMRED ISSN: 0105-2896
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 100

It is clear by now that cell-to-cell interactions involving a variety of signals are required for effective immune response. The data reviewed here suggest that CD40-CD40L interactions are critical for development of CD4 T-cell-dependent effector functions. Lack of this important interaction results in greatly reduced activation of CD4 T cells, while successful interaction of these molecules results in full activation of these T cells. Consequently, the absence of CD40-CD40L interactions leads to impairment of T-cell effector such as help for B-cell differentiation and class switch, activation of monocytes and macrophages to produce cytokines and to kill intracellular pathogens, and activation of autoreactive T cells to mount an autoimmune response. The effector functions of T cells controlled by CD40-CD40L interactions in a successful immune response are given in Table I. Data presented so far suggest that ***CD40*** -CD40L interactions play a role in early signalling events, where interactions of this kind are required to induce expression of costimulatory molecules on APC. One possible sequence of events is that APC, like DC, take up antigens at the site of injury or infection and migrate to lymph nodes, where they present antigens complexed with MHC class II molecules to naive T cells. This results in expression of CD40L on T cells. Coupling of this newly expressed CD40L on T cells with CD40 on APC results in expression of the costimulatory activity of the APC. At this time the costimulatory signal provided by the APC is received by the T cell via CD28/CTLA-4, which drives the cell to enter into cell cycle and complete T cell activation. T cells thereby activated can now enter into secondary cognate CD40-CD40L-dependent effector recognition with B cells to switch Ig class, macrophages to produce cytokines and new DC carrying the same antigen to up-regulate costimulatory activity. A tight regulation of expression of CD40L on T cells and costimulatory activity on APC would prevent activation of unwanted bystander T cells. The coupling of activation of the APC primed with the cognate antigen to the activation of the T-cell specific for that antigen in this model provides an additional regulatory step in the initiation of the immune response. This also suggests that a limited number of T cells/APC will be activated, both of which will be specific in nature. This additional step may be important for safeguarding against an autoimmune response. In addition, the fact that CD40L uniquely seems to play this role suggests that selective immunotherapies to treat autoimmune disease and prevent graft rejection can be targeted on this molecule. On the other hand, ***CD40*** -directed approaches to up-regulate costimulatory activity on APC could be developed to fight tumor growth, contain infections and treat immunodeficiencies.

06690640 EMBASE No: 1996355574
Induction of cognate and non-cognate T-cell help for B-cell IgE

production in relation to CD40 ligand expression
Armerding D.; Hren A.; Callard R.E.; Fu S.M.; Mudde G.C.
Harvard Skin Disease Research Center, Division of Dermatology, Brigham Woman Hosp, Harvard Med Schl, 75 Francis Street,Boston, MA 02115 United States
International Archives of Allergy and Immunology (INT. ARCH. ALLERGY IMMUNOL.) (Switzerland) 1996, 111/4 (376-384)
CODEN: IAAIE ISSN: 1018-2438
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Nonactivated, fixed peripheral blood T cells (PBT) from healthy donors or patients with X-linked-hyper-IgM (HIGM) syndrome, or cloned T cells provided effective help for tonsillar B lymphocytes for induction of IgE or other immunoglobulin (Ig) isotypes. Helper activity was mediated by staphylococcal superantigens adsorbed to the T cells prior to fixation and required presence of IL-4 in the cultures. We demonstrated that the T cells neither expressed detectable CD40 ligand at the beginning of the superantigen treatment nor 24 h later. Phorbol ester (PMA) plus Ca-ionophore treatment efficiently induced CD40L. Such T cells did not, however, provide any help for B-cell activation in some experiments or stimulated only low responses in others. Antibodies against CD2, CD3 and ICAM-1 adsorbed to fixed T cells prior to coculturing inhibited helper activity. A soluble ***CTLA4*** construct was also inhibitory. Our results suggest a pathway of B-cell activation independent of CD40L expressed on T cells.

30/7/5 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

06547485 EMBASE No: 1996207829
Development of B-cell memory and effector function
Lane P.
Basel Institute for Immunology, Grenzacherstrasse 487,Basel CH-4005 Switzerland
Current Opinion in Immunology (CURR. OPIN. IMMUNOL.) (United Kingdom) 1996, 8/3 (331-335)
CODEN: COPIE ISSN: 0952-7915
DOCUMENT TYPE: Journal; Short Survey
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The past year has seen significant advances in our understanding of molecules that both positively and negatively regulate B- and T-cell responses. Of particular interest is the lethal phenotype of ***CTLA*** -4-deficient mice, which has illuminated the importance of downregulation of T-cell responses and the increasingly complicated role of ***CD40*** and its ligand in directing both T- and B-cell priming.

30/7/6 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06530789 EMBASE No: 1996194278
Suppression of murine allergic contact dermatitis by CTLA4Ig: Tolerance induction of Th2 responses requires additional blockade of CD40-ligand
Tang A.; Judge T.A.; Nickoloff B.J.; Turka L.A.
Department of Medicine, 409-A Stellar-Chance Building, University of Pennsylvania, 422 Curie Boulevard,Philadelphia, PA 19104-6069 United States
Journal of Immunology (J. IMMUNOL.) (United States) 1996, 157/1

(117-125)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Blockade of costimulation through the B7-CD28 pathway by CTLA4Ig can lead to Ag-specific T cell tolerance. Most models studied to date involve a Th1- dependent response. To investigate whether the tolerizing effects of CTLA4Ig might vary depending upon the cytokine nature of the immune response, we studied its effects on contact hypersensitivity (CHS) in response to two allergens. In BALB/c mice, both 2,4-dinitrofluorobenzene (DNFB) and FITC induce CHS. However, the DNFB response is Th1-predominant, while the FITC response is Th2 predominant. CTLA4Ig treatment during primary sensitization induced long-lasting unresponsiveness to DNFB, with 88% and 76% inhibition of primary (first challenge) and secondary (re-sensitization and re-challenge) CHS, respectively. In contrast, ***CTLA4Ig*** inhibited primary CHS to FITC by over 82% but had little effect on secondary CHS. Consistent with its effects on CHS, the suppressive effect of CTLA4Ig on Th2 cells was short-lived in FITC- sensitized mice, while Th1-like cytokine-secreting cells remained reduced in DNFB-sensitized mice, even when the animals were rechallenged with DNFB. The addition of anti-CD40L Ab to ***CTLA4Ig*** was able to induce long-lasting unresponsiveness to FITC, indicating the ability of cells mounting this Th2 response to receive costimulatory signals through either pathway. In conclusion, CHS can be mediated by both Th1 and Th2 cells, and the ability of CTLA4Ig to lead to long-standing nonresponsiveness in this model depends on the nature (i.e., cytokine profile) of the immune response.

30/7/7 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

06506165 EMBASE No: 1996163338
Signaling through CD28/CTLA-4 family receptors: Puzzling participation of phosphatidylinositol-3 kinase
Hutchcroft J.E.; Bierer B.E.
Division of Pediatric Oncology, Dana-Farber Cancer Institute, Dana 1710, 44 Binney Street,Boston, MA 02115 United States
Journal of Immunology (J. IMMUNOL.) (United States) 1996, 156/11 (4071-4074)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Note
LANGUAGE: ENGLISH

30/7/8 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

06474891 EMBASE No: 1996137577
Distinct regulatory roles of lymphocyte costimulatory pathways on T helper type 2-mediated autoimmune disease
Biancone L.; Andres G.; Ahn H.; Lim A.; Dai C.; Noelle R.; Yagita H.; De Martino C.; Stamenkovic I.
Department of Pathology, Harvard Med. School/Pathology Res., Massachusetts General Hospital, 149 13th Street,Boston, MA 02129 United States
Journal of Experimental Medicine (J. EXP. MED.) (United States) 1996, 183/4 (1473-1481)
CODEN: JEMEA ISSN: 0022-1007
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We assessed the role of CD40-CD40L, cytotoxic T lymphocyte (CTL)A4/CD28- B7s, and CD2-CD48/CD58 lymphocyte costimulatory pathways in the development of mercury chloride (HgClinf 2)-induced autoimmune disease in mice, which is believed to be mediated by T helper (Th) subset Th2. Inhibition of CD40- CD40L and CTLA4/CD28-B7s interactions by anti-CD40L antibody and soluble CTLA4-immunoglobulin (Ig) fusion protein, respectively, abrogated the autoimmune disease without affecting interleukin 4 (IL-4) production, showing the importance of physical contact between T and B lymphocytes in the Th2- mediated process. In contrast, two anti-CD2 antibodies that have been shown to induce immunosuppression of Th1-mediated events exacerbated the autoantibody response and augmented IgG1, IgE, and IL-4 production, transforming a mild mesangial glomerulopathy into a severe systemic immune complex disease. These observations demonstrate that manipulation of lymphocyte accessory counterreceptor interactions may affect the course of Th2-associated autoimmune disease and suggest that signals resulting from CD2 engagement may play an essential role in the regulation of the Th1-Th2 effector equilibrium.

30/7/9 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

06454794 EMBASE No: 1996119616
The relative contribution of the CD28 and gp39 costimulatory pathways in the clonal expansion and pathogenic acquisition of self-reactive T cells
Griggs N.D.; Agersborg S.S.; Noelle R.J.; Ledbetter J.A.; Linsley P.S.; Tung K.S.K.
Department of Pathology, University of Virginia, Box 214,Charlottesville, VA 22908 United States
Journal of Experimental Medicine (J. EXP. MED.) (United States) 1996, 183/3 (801-810)
CODEN: JEMEA ISSN: 0022-1007
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The zona pellucida (ZP), an ovarian extracellular structure, contains three major glycoproteins; ZP1, ZP2, and ZP3. A ZP3 peptide contains both an autoimmune oophoritis-inducing T cell epitope and a B cell epitope that induces autoantibody to ZP. This study investigates two major T cell costimulation pathways in this disease model. Herein we show that blockage of glycoprotein (gp)39 and CD40 interaction with gp39 monoclonal antibody (mAb) results in the failure to induce both autoimmune oophoritis and autoantibody production. Inhibition of ligand binding to the CD28 receptor with the fusion protein, murine, CTLA4-Ig-immunoglobulin (Ig), also results in failure to generate antibody to ZP and significantly reduces diseases severity and prevalence. Surprisingly, the frequencies of antigen-specific T cells in anti-gp39 mAb-treated mice, CTLA4-Ig treated mice, and in mice given control hamster IgG or control fusion protein L6, were equivalent as determined by limiting dilution analysis (approx. eq.1:5,000). These T cells, which produced comparable amounts of interleukin 4 and interferon gamma in vitro, were able to transfer oophoritis to normal recipients. When anti-gp39 mAb and ***CTLA4*** -Ig were given together, the effect was additive, leading to inhibition of T cell activation as determined by in vitro proliferation and limiting dilution analysis (approx. eq.1:190,000); disease and antibody responses were absent in these mice. By studying these two costimulatory pathways in parallel, we have shown that autoimmune disease and autoantibody production are inhibitable by blocking either the gp39 or the CD28 pathway, whereas inhibition of clonal expansion of the effector T cell population occurs only when both pathways are blocked.

30/7/10 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

06390997 EMBASE No: 1996054635
Regulation of CD40 ligand expression on naive CD4 T cells: A role for TCR but not co-stimulatory signals
Jaiswal A.I.; Dubey C.; Swain S.L.; Croft M.
Department of Biology, University of California San Diego, 9500 Gilman Drive,La Jolla, CA 92093-0063 United States
International Immunology (INT. IMMUNOL.) (United Kingdom) 1996, 8/2 (275-285)
CODEN: INIME ISSN: 0953-8178
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We have investigated the roles of TCR and accessory co-stimulatory signals in the induction of ***CD40*** ligand (CD40L) on CD4 cells. Using naive T cells from TCR transgenic mice, specific for a peptide of pigeon cytochrome c, we show that in contrast to IL-2 secretion, CD40L expression is regulated primarily by signaling through the TCR, is enhanced by accessory molecule interactions, but co-stimulatory signals play little if any role. CD40L was induced at high levels on naive T cells, peaking at 5 h, by class II MHCsup + fibroblast antigen-presenting cells (APC) which expressed either ICAM-1, B7-1 or both molecules, whereas only low levels were induced by fibroblasts which did not express any accessory molecules. Differences in intensity and duration of expression were seen following stimulation with ICAM- and B7-expressing APC, with the presence of ICAM resulting in greater and longer expression, although both molecules together were most efficient. The involvement of co-stimulatory signals delivered from accessory molecules was investigated in systems where there was no effect on TCR signaling from adhesive interactions. Anti-CD3, or antigen-pulsed APC lacking accessory molecules, were used to provide the TCR signal, with co-stimulus from either anti-CD28 or accessory molecule-expressing fibroblasts not presenting antigen. Anti-CD3 in the absence of co-stimuli induced high CD40L expression but no IL-2 production and provision of co-stimulatory signals, although inducing large quantities of IL-2, did not increase CD40L expression. In addition, low CD40L expression induced by antigen presented in the absence of accessory molecules was not enhanced by co-stimulation, although IL-2 was strongly up-regulated. These studies suggest that efficient expression of CD40L on naive CD4 cells does require accessory molecules on APC. However, the role of these molecules for CD40L induction, as opposed to IL-2 secretion, is not one of co-stimulation but one of adhesion, presumably allowing stronger or more prolonged signals to be generated through the TCR. The synergistic role of ICAM and B7 during naive CD4 activation was confirmed using dendritic cells as APC, with nearly complete inhibition of CD40L expression as well as IL-2 secretion being seen when both CTLA-4-Ig and anti-LFA-1 were used to block these molecules.

30/7/11 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11070227 PMID: 8892665
Differential effect of CTLA4Ig on murine graft-versus-host disease (GVHD) development: CTLA4Ig prevents both acute and chronic GVHD development but reverses only chronic GVHD.
Via C S; Rus V; Nguyen P; Linsley P; Gause W C
Research Service, Baltimore VA Medical Center, University of Maryland School of Medicine 21201, USA.
Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Nov 1

1996, 157 (9) p4258-67, ISSN 0022-1767--Print Journal Code: 2985117R
Contract/Grant Number: R29 AI33882; AI; NIAID
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The role of costimulation was examined in an in vivo model of alloantigen-driven Th1 or Th2 cytokine responses, the parent-into-F1 model of acute or chronic ***graft*** -vs-host disease (GVHD), respectively. The soluble fusion protein, murine CTLA4Ig, which blocks engagement of CD28 by its natural ligand B7-1 and B7-2, was administered either early, at the time of GVHD induction, or delayed, after the establishment of Th1 or Th2 effector responses (day 7). Early administration of ***CTLA4Ig*** prevented the development of both acute and chronic GVHD by preventing the activation of donor T cells, i.e., by blocking characteristic Th1 or Th2 cytokine production and blocking memory marker up-regulation on donor T cells. Delayed ***CTLA4Ig*** administration was unable to alter acute GVHD but did reverse chronic GVHD as evidenced by normalization of serum autoantibody levels, normal host B cell numbers and MHC class II expression, reduced donor T cell expression of CD40 ligand, and reduced numbers of donor CD4+ memory T cells. The percentage of donor memory cells was not altered by delayed ***CTLA4Ig*** . We conclude that in this model, alloantigen-driven Th1 or Th2 responses are equally susceptible to costimulatory blockade at the onset of disease; however, once effector mechanisms become established, only Th2-driven responses have a requirement for further costimulation for the continued expansion of CD4+ T cells. These data suggest that humoral, lupus-like autoimmunity requires continuous T cell help for B cells, and agents that interrupt this process may be beneficial.
Record Date Created: 19961213
Record Date Completed: 19961213

30/7/12 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

126017804 CA: 126(2)17804h PATENT
Human antibodies derived from immunized xenomice
INVENTOR(AUTHOR): Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J.
LOCATION: USA
ASSIGNEE: Cell Genesys, Inc.
PATENT: PCT International ; WO 9634096 A1 DATE: 19961031
APPLICATION: WO 95US5500 (19950428)
PAGES: 64 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: C12N-015/00A
DESIGNATED COUNTRIES: AU; CA; FI; HU; JP; KR; NO; NZ
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA215003 Immunochemistry
IDENTIFIERS: human antibody Ig xenomice therapeutic
DESCRIPTORS:
Proteins(specific proteins and subclasses)...
amadori; human antibodies derived from immunized xenomice
Dermatophagoides... Leukocyte...
antigen; human antibodies derived from immunized xenomice
Antigens...

A7; human antibodies derived from immunized xenomice
Interferon receptors...
β; human antibodies derived from immunized xenomice
Antigens...
B7.3; human antibodies derived from immunized xenomice
CD antigens...
CDw52; human antibodies derived from immunized xenomice
CD antigens...
CD27; human antibodies derived from immunized xenomice
Antigens...
CD29 ligand; human antibodies derived from immunized xenomice
Antigens...
CD30 ligand; human antibodies derived from immunized xenomice
CD antigens...
CD6; human antibodies derived from immunized xenomice
CD antigens...
CD72; human antibodies derived from immunized xenomice
Fc receptors...
E; human antibodies derived from immunized xenomice
Sialoglycoproteins...
endosialins; human antibodies derived from immunized xenomice
Glycoproteins(specific proteins and subclasses)...
gcIII; human antibodies derived from immunized xenomice
Lipids,biological studies...
glycated; human antibodies derived from immunized xenomice
Glycoproteins(specific proteins and subclasses)...
gp39; human antibodies derived from immunized xenomice
Cytokines...
Groα; human antibodies derived from immunized xenomice
Cytokines...
Groβ; human antibodies derived from immunized xenomice
Myelin...
growth inhibitor associated with; human antibodies derived from immunized xenomice
Thyroid diseases...
Hashimoto's thyroiditis; human antibodies derived from immunized xenomice
Surface antigens...
hepatitis virus; human antibodies derived from immunized xenomice
Adult respiratory distress syndrome... Allergens... Animal cell line... Animal cells... Antibodies... Antigens... Asthma... Autoimmune diseases... B cell(lymphocyte)... Behcet's syndrome... Cachexia... Carcinoembryonic antigen... CD11a(antigen)... CD11b(antigen)... CD11c(antigen)... CD14(antigen)... CD19(antigen)... CD20(antigen)... CD22(antigen)... CD28(antigen)... CD2(antigen)... CD30(antigen)... CD3(antigen)... CD40 ligand... CD40(antigen)... CD44(antigen)... CD45(antigen)... CD4(antigen) ... CD56(antigen)... CD5(antigen)... CD69(antigen)... CD7(antigen)... CD80(antigen)... CD86(antigen)... CD8(antigen)... Cell adhesion molecules ... Chemokines... Cholesteryl ester transfer protein... Class I MHC antigens... Class II MHC antigens... Coagulation factors(blood)... CTLA-4(antigen)... Cytomegalovirus... Dermatomyositis... Diagnosis... E glycoprotein(envelope glycoprotein)... Endotoxins... Enzymes,biological studies... Eosinophil cationic protein... Epidermal growth factor receptors ... Erythropoietin receptors... E-selectin... Fas antigen... Fc receptors ... FcεRI receptors... FcεRII receptors... Fibrinogens... Fibrins... Fibroblast growth factor receptors... Glomerulonephritis... Glycoprotein B... Glycoprotein H... Graft-vs.-host reaction... Granulocyte colony-stimulating factor receptors... Graves' disease... Growth factor receptors... Growth factors(animal)... Hematopoietin receptors... Hepatitis virus... Histocompatibility antigens... Human herpesvirus 3... Human herpesvirus 4... Human herpesvirus... Human immunodeficiency virus 1... Human papillomavirus... ICAM-1(cell adhesion molecule)... ICAM-2(cell adhesion molecule)... IgE... Immunoglobulins... Insulin-dependent diabetes mellitus... Integrin α1β1... Integrin α2β1...

Integrin α3β1... Integrin α4β1... Integrin α5β1... Integrin α6β1... Integrin β1... Integrin β2... Interferon receptors... Interferon α receptors... Interferon γ receptors... Interferon γ... Interleukin receptors ... Interleukin 1 receptors... Interleukin 10... Interleukin 11... Interleukin 12... Interleukin 13... Interleukin 15... Interleukin 1... Interleukin 2 receptors... Interleukin 2... Interleukin 3 receptors... Interleukin 3... Interleukin 4 receptors... Interleukin 4... Interleukin 5 receptors... Interleukin 5... Interleukin 6 receptors... Interleukin 6... Interleukin 7 receptors... Interleukin 7... Interleukin 8 receptors... Interleukin 8... Interleukin 9... Interleukins... Ley antigen... LFA-1(antigen)... LFA-3(antigen)... L-selectin... Macrophage inflammatory protein 1α... Mac-1 antigen... Major basic protein... Metastasis(tumor)... Monoclonal antibodies... Monocyte chemoattractant protein-1... Mucins... Multiple myeloma... Multiple sclerosis... Myasthenia gravis... Neutrophil-activating peptide-2... Osteopontin... Osteoporosis... Oxidized low-density lipoproteins... Paget's disease of bone... Platelet-derived growth factor receptors... Platelet-derived growth factors ... Polymyositis... Pseudomonas... Psoriasis... p150,95 antigen... P-glycoproteins... P-selectin... RANTES(chemokine)... Renal cell carcinoma ... Reperfusion injury... Respiratory syncytial virus... Rh blood groups... Rheumatoid arthritis... Scleroderma... Septic shock... Sjogren's syndrome ... Systemic lupus erythematosus... TCR(T-cell receptors)... Tetanus toxin ... Therapy... Thyrotropin receptors... Toxins... Transforming growth factor β receptors... Transforming growth factors β... Tumor necrosis factor receptors... Tumor necrosis factor α... Tumor-associated antigen... Type IV collagen... VCAM-1(cell adhesion molecule)...

human antibodies derived from immunized xenomice

Parathyroid hormone receptors...

humoral hypercalcemic factor; human antibodies derived from immunized xenomice

Genes(animal)...

Ig.; human antibodies derived from immunized xenomice

Interleukin receptors...

interleukin 10 receptors; human antibodies derived from immunized xenomice

Interleukin receptors...

interleukin 11 receptors; human antibodies derived from immunized xenomice

Interleukin receptors...

interleukin 13 receptors; human antibodies derived from immunized xenomice

Interleukins... Receptors...

interleukin 14; human antibodies derived from immunized xenomice

Interleukin receptors...

interleukin 15 receptors; human antibodies derived from immunized xenomice

Interleukin receptors...

interleukin 9 receptors; human antibodies derived from immunized xenomice

Lewis blood groups...

Leb, synthetic; human antibodies derived from immunized xenomice

Selectins...

ligands; human antibodies derived from immunized xenomice

Proteins(specific proteins and subclasses)...

LMP-1; human antibodies derived from immunized xenomice

Membrane proteins...

LMP-2 (latent-infection membrane protein 2); human antibodies derived from immunized xenomice

Allergens...

Lol p I (Lolium perenne, I); human antibodies derived from immunized xenomice

Connective tissue diseases...

mixed; human antibodies derived from immunized xenomice
Skin diseases...
Paget disease; human antibodies derived from immunized xenomice
Breast diseases... Reproductive tract diseases...
Paget; human antibodies derived from immunized xenomice
Antibodies...
pANCA or perinuclear antineutrophil cytoplasm antibodies; human antibodies derived from immunized xenomice
Skin diseases...
pemphigus; human antibodies derived from immunized xenomice
Chemokines...
PF4; human antibodies derived from immunized xenomice
c-erbB2 gene(animal)...
products; human antibodies derived from immunized xenomice
Virus...
protein; human antibodies derived from immunized xenomice
IgE... Interleukin 11... Interleukin 12... Interleukin 13... Interleukin 15 ... Interleukin 9...
receptors; human antibodies derived from immunized xenomice
DNA...
recombinant; human antibodies derived from immunized xenomice
Arthritis... Conjunctivitis... Urinary tract diseases...
Reiter's syndrome; human antibodies derived from immunized xenomice
Transplant(organ)...
rejection; human antibodies derived from immunized xenomice
Ischemia...
reperfusion; human antibodies derived from immunized xenomice
Ligands...
selectin; human antibodies derived from immunized xenomice
Venoms...
snake; human antibodies derived from immunized xenomice
Proteins(specific proteins and subclasses)...
uropontins; human antibodies derived from immunized xenomice
Receptors...
vascular endothelial growth factor; human antibodies derived from immunized xenomice
Bee... Snake...
venom; human antibodies derived from immunized xenomice
Proteins (general),biological studies...
viral; human antibodies derived from immunized xenomice
Mouse...
xeno-; human antibodies derived from immunized xenomice
Interleukin receptors...
12; human antibodies derived from immunized xenomice
CAS REGISTRY NUMBERS:
90027-15-3 90245-82-3 90546-31-3 196000-12-3 532375-95-3 620103-71-3
620315-43-3 622295-09-3 800435-34-3 802954-38-3 802955-41-3
816697-07-3 829868-98-3 924482-21-3 986038-40-3 1162437-33-3
1274646-02-3 human antibodies derived from immunized xenomice
90026-46-3 proteins related to; human antibodies derived from immunized xenomice

30/7/13 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

125326411 CA: 125(25)326411q PATENT
Inhibiting rejection of a graft
INVENTOR(AUTHOR): Strom, Terry B.
LOCATION: USA
ASSIGNEE: Beth Israel Hospital Association
PATENT: PCT International ; WO 9631229 A1 DATE: 961010
APPLICATION: WO 96US4717 (960405) *US 417077 (950405)

PAGES: 45 pp CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: A61K-038/18A; A61K-038/19B; C07K-014/475B; C07K-014/52B
DESIGNATED COUNTRIES: CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES ; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
SECTION:
CA215002 Immunochemistry
IDENTIFIERS: antigen presenting cell costimulatory protein chimera, graft rejection chimeric polypeptide
DESCRIPTORS:
Heart...
brain-dead donor; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Antigens...
B7-3; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Antigens...
CD48; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Albumins,biological studies... Antibodies,monoclonal... Antigens,B 7.2... Antigens,B7/BB-1... Antigens,CD28... Antigens,CD2... Antigens,CD40... Antigens,CD58... Antigens,CTLA-4 (cytotoxic T-lymphocyte-activating, 4)... Glycoproteins,specific or class, CD40-L (antigen CD40 ligand)... Immunoglobulin receptors,FcR (Ig fragment Fc receptor)... Immunoglobulins,G ... Immunological accessory cell... Lymphocyte,T-cell... Proteins,specific or class... Receptors,FcR (Ig fragment Fc receptor)...
chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Peptides,biological studies... Proteins,biological studies...
chimeric; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Brain...
dead; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Complement...
fixation; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Antigens...
graft rejection; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
Transplant and Transplantation,graft-vs.-host reaction...
inhibition; chimeric polypeptide that binds to costimulatory protein of antigen-presenting cell is disclosed for inhibiting graft rejection
?

Gambel, Phillip

To: STIC-EIC1600/2900
Subject: anti-ctla antibodies and autoimmunity / 10/732847

stic

please provide the following references to

phillip gambel
art unit 1644
272-0844

1644 mailbox 3c70

thanx

********** **10/732847**********

4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0019791103 BIOSIS NO.: 200700450844
Inhibition of T cell activation and autoimmune diabetes using a B cell surface-linked CTLA-4 agonist
AUTHOR: Fife Brian T; Griffin Matthew D; Abbas Abul K; Locksley Richard M; Bluestone Jeffrey A (Reprint)
AUTHOR ADDRESS: Univ Calif San Francisco, Ctr Diabet, Dept Med, 513 Parnassus Ave,Box 0540, San Francisco, CA 94143 USA**USA
AUTHOR E-MAIL ADDRESS: jbluest@diabetes.ucsf.edu
JOURNAL: Journal of Clinical Investigation 116 (8): p2252-2261 AUG 2006 2006
ISSN: 0021-9738
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CTL-associated antigen 4 (CTLA-4) engagement negatively regulates T cell activation and function and promotes immune tolerance. However, it has been difficult to explore the biology of selective engagement of CTLA-4 in vivo because CTLA-4 shares its ligands, B7-1 and B7-2, with CD28. To address this issue, we developed a Tg mouse expressing a single-chain, membrane-bound anti-CTLA-4 Ab (scFv) on B cells. B and T cells developed normally and exhibited normal phenotype in the steady state and after activation in these mice. However, B cells from scFv Tg(+) mice (scaCTLA4(+)) prevented T cell proliferation and

cytokine production in mixed lymphocyte reactions. Additionally, mice treated with scaCTLA4+ B cells had decreased T cell-dependent B cell Ab production and class switching in vivo after antigen challenge. Furthermore, expression of this CTLA-4 agonist protected NOD mice from spontaneous autoimmune diabetes. Finally, this disease prevention occurred in Treg-deficient NOD.B7-1/B7-2 double-knockout mice, suggesting that the effect of the CTLA-4 agonist directly attenuates autoreactive T cell activation, not Treg activation. Together, results from this study demonstrate that selective ligation of CTLA-4 attenuates in vivo T cell responses, prevents development of autoimmunity, and represents a novel immunotherapeutic approach for the induction and maintenance of peripheral tolerance.

********** **10/732847** **********

********** **10/732847** **********

4/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

17297991 BIOSIS NO.: 200300256710
Targeted engagement of CTLA-4 prevents autoimmune thyroiditis.
AUTHOR: Vasu Chenthamarakshan; Gorla Seema R; Prabhakar Bellur S; Holterman Mark J (Reprint)
AUTHOR ADDRESS: Department of Surgery, University of Illinois at Chicago, Chicago, IL, 60612, USA**USA
AUTHOR E-MAIL ADDRESS: rmasjet@uic.edu
JOURNAL: International Immunology 15 (5): p641-654 May 2003 2003
MEDIUM: print
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The CTLA-4-mediated signal is a critical step in the down-modulation of immune responses. The therapeutic potential of this signal to induce tissue-specific tolerance was investigated by using an anti-CTLA-4 antibody that was coupled to an antibody specific for the thyrotropin receptor. After in vivo administration, this bispecific antibody (BiAb) accumulated in the thyroid and prevented development of experimental autoimmune thyroiditis (EAT) in mice immunized with mouse thyroglobulin (mTg). Lymphocytes from BiAb-treated mice showed a significant reduction in their ability to proliferate, and to produce IL-2, IFN-gamma and tumor necrosis factor (TNF)-alpha, in response to mTg re-stimulation compared to lymphocytes from untreated mice. Moreover, BiAb-treated mice showed suppressed anti-mTg antibody response, lymphocytic infiltration of the thyroid and follicular destruction. The BiAb targeted to the thyroid most likely facilitated engagement of CTLA-4, resulting in an increase in the number of CD4+CD25+ T cells. These regulatory T cells suppressed in vitro mTg-specific T cell responses, which were associated with an enhanced transforming growth factor (TGF)-beta1 production. Neutralization of TGF-beta1 increased mTg-specific in vitro proliferation of, and IL-2 production by, T cells from BiAb-treated mice. Our data suggest that engagement of CTLA-4 expressed on activated autoreactive T cells in close proximity to the

thyroid can increase the number of regulatory T cells and their ability to produce TGF-beta1, with a concomitant reduction in IFN-gamma and TNF-alpha, resulting in suppression of EAT.

********** 10/732847**********

4/7/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16680032 BIOSIS NO.: 200200273543
The role of CTLA-4 in induction and maintenance of peripheral T cell tolerance
AUTHOR: Eagar Todd N; Karandikar Nitin J; Bluestone Jeffrey A; Miller Stephen D (Reprint)
AUTHOR ADDRESS: Department of Microbiology-Immunology, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL, 60611, USA**USA
JOURNAL: European Journal of Immunology 32 (4): p972-981 April, 2002 2002
MEDIUM: print
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: T cell receptor engagement and the B7-CD28/CTLA-4 signaling pathways play critical roles in T cell activation and regulation. CD28 engagement results in T cell activation, differentiation and survival while CTLA-4 signals block IL-2 production, cell cycle progression and T cell differentiation. We explored the role of CTLA-4 in peripheral tolerance induced by intravenous administration of ethylene carbodiimide-fixed, antigen-coupled splenocytes in the PLP139-151-induced relapsing experimental autoimmune encephalomyelitis system. Tolerance induction with PLP139-151-coupled splenocytes correlates with low B7 expression on the fixed antigen-presenting cells, conditions that would favor CTLA-4-mediated inhibition. Administration of CTLA-4Ig or anti-CTLA-4 concomitant with the 'tolerogenic' stimulus, however, failed to reverse tolerance induction. In contrast, blocking CTLA-4 at the time of secondary 'immunogenic' encounter with antigen reversed the tolerant state. These findings indicate that CTLA-4 is required to maintain the unresponsive state of the tolerized T cells upon antigenic stimulation under inflammatory conditions and, therefore, have important implications for therapeutic regulation of autoimmune disease.

********** 10/732847**********

4/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16397083 BIOSIS NO.: 200100568922
Targeted delivery of anti-CTLA-4 antibody downregulates T cell function in vitro and in vivo
AUTHOR: Rao Seema; Vasu Chenthamarakshan; Martinez Osvaldo; Kaithamana Shashi; Prabhakar Bellur S; Holterman Mark J (Reprint)
AUTHOR ADDRESS: Division of Pediatric Surgery, Department of Surgery,

College of Medicine, University of Illinois at Chicago, Chicago, IL, 60612, USA**USA

JOURNAL: Clinical Immunology (Orlando) 101 (2): p136-145 November, 2001 2001

MEDIUM: print

ISSN: 1521-6616

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CTLA-4 is a T cell surface molecule that binds to the costimulatory molecules CD80 and CD86 on antigen-presenting cells and downregulates T cell function. Therefore, we wanted to test whether antigen-specific activated T cells could be inhibited through directed CTLA-4 signaling using a bispecific antibody (BiAb) capable of simultaneously binding to CTLA-4 and a tissue-specific antigen. The BiAb was prepared by linking two separate monoclonal antibodies against CTLA-4 and the thyroid-stimulating hormone receptor (TSHR). The mouse B cell lymphoma line M12 (H2d) was used to induce alloreactive T cells in CBA/J mice (H2k); M12 cells stably transfected with the cDNA encoding murine TSHR (mM12) were used to restimulate the alloresponse in vitro. Results of assays for in vitro T cell proliferation, IL-2 production, and cytotoxicity in the presence of BiAb demonstrated that the BiAb could inhibit the T cell alloresponse when stimulated with mM12 cells but not with M12 cells. This effect was dependent on binding of TSHR-bound BiAb to CTLA-4, since the addition of soluble CTLA-4-Ig blocked the inhibitory effect. Injection of mM12 cells, along with the BiAb, not with antibodies against TSHR or CTLA-4 either separately or together, into CBA/J mice (H2k) downregulated alloreactive T cell responses. Our study demonstrated that the presence of CTLA-4 signaling molecules on the surface of target cells can protect those cells from immune attack by antigen-specific T cells and suggested that a similar approach could have potential therapeutic value in transplant rejection and tissue-specific autoimmune diseases.

********** **10/732847**********

6/3/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13453821 BIOSIS NO.: 199699087881
CTLA-4 engagement inhibits IL-2 accumulation and cell cycle progression upon activation of resting T cells
AUTHOR: Krummel Matthew F; Allison James P (Reprint)
AUTHOR ADDRESS: Cancer Res Lab., 447 Life Sci. Addition, Univ. Calfironia, Berkeley, CA 94720, USA**USA

JOURNAL: Journal of Experimental Medicine 183 (6): p2533-2540 1996 1996

ISSN: 0022-1007

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

********** **10/732847**********

6/7/22 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

136048180 CA: 136(4)48180n JOURNAL
Immunotoxins containing recombinant anti-CTLA-4 single-chain fragment variable antibodies and saporin: in vitro results and in vivo effects in an acute rejection model
AUTHOR(S): Tazzari, Pier-Luigi; Polito, Letizia; Bolognesi, Andrea; Pistillo, Maria-Pia; Capanni, Paolo; Palmisano, Giulio Lelio; Lemoli, Roberto M.; Curti, Antonio; Biancone, Luigi; Camussi, Giovanni; Conte, Roberto; Ferrara, Giovanni B.; Stirpe, Fiorenzo
LOCATION: Service of Transfusion Medicine, S. Orsola-Malpighi Hospital, Bologna, Italy
JOURNAL: J. Immunol. DATE: 2001 VOLUME: 167 NUMBER: 8 PAGES: 4222-4229 CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists
SECTION:
CA201007 Pharmacology
IDENTIFIERS: immunotoxin CTLA4 antibody saporin immunosuppression antitumor
DESCRIPTORS:
T cell(lymphocyte)...
activation; immunotoxins contg. recombinant anti-CTLA-4 single-chain variable fragment antibodies and saporin for immunotherapy
Immunoglobulins...
fragments, Fv; immunotoxins contg. recombinant anti-CTLA-4 single-chain variable fragment antibodies and saporin for immunotherapy
Antitumor agents... Apoptosis... CTLA-4(antigen)... Immunosuppressants...
Immunotherapy...
immunotoxins contg. recombinant anti-CTLA-4 single-chain variable fragment antibodies and saporin for immunotherapy
Drug delivery systems...
immunotoxins; immunotoxins contg. recombinant anti-CTLA-4 single-chain variable fragment antibodies and saporin for immunotherapy
Proteins...
saporins; immunotoxins contg. recombinant anti-CTLA-4 single-chain variable fragment antibodies and saporin for immunotherapy
Antibodies...
single chain; immunotoxins contg. recombinant anti-CTLA-4 single-chain variable fragment antibodies and saporin for immunotherapy

********** **10/732847** **********

4/7/24 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

15870213 BIOSIS NO.: 200100042052
Therapy for autoimmune thyroiditis: Immunomodulation of autoreactive T cells via CTLA4 signaling
AUTHOR: Rao S (Reprint); Chenthamarakshan V (Reprint); Martinez O (Reprint); Kaithamana S (Reprint); Prabhakar B S (Reprint); Holterman M J (Reprint)
AUTHOR ADDRESS: University of Illinois at Chicago, Chicago, IL, 60612, USA
**USA
JOURNAL: FASEB Journal 14 (6): pA1079 April 20, 2000 2000

MEDIUM: print
CONFERENCE/MEETING: Joint Annual Meeting of the American Association of Immunologists and the Clinical Immunology Society Seattle, Washington, USA May 12-16, 2000; 20000512
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

********** **10/732847**********

4/7/39 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

13427536 EMBASE No: 2005497259
Human CTLA4 knock-in mice unravel the quantitative link between tumor immunity and autoimmunity induced by anti-CTLA-4 antibodies
Lute K.D.; May Jr. K.F.; Lu P.; Zhang H.; Kocak E.; Mosinger B.; Wolford C.; Phillips G.; Caligiuri M.A.; Zheng P.; Liu Y.
Y. Liu, Department of Pathology, Ohio State University Medical Center, 129 Hamilton Hall, 1645 Neil Ave, Columbus, OH 43210 United States
AUTHOR EMAIL: liu-3@medctr.osu.edu
Blood (BLOOD) (United States) 2005, 106/9 (3127-3133)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

Although results from preclinical studies in animal models have proven the concept for use of anti-cytotoxic T-lymphocyte antigen 4 (CTLA-4) antibodies in cancer immunotherapy, 2 major obstacles have hindered their successful application for human cancer therapy. First, the lack of in vitro correlates of the antitumor effect of the antibodies makes it difficult to screen for the most efficacious antibody by in vitro analysis. Second, significant autoimmune side effects have been observed in a recent clinical trial. In order to address these 2 issues, we have generated human CTLA4 gene knock-in mice and used them to compare a panel of anti-human CTLA-4 antibodies for their ability to induce tumor rejection and autoimmunity. Surprisingly, while all antibodies induced protection against cancer and demonstrated some autoimmune side effects, the antibody that induced the strongest protection also induced the least autoimmune side effects. These results demonstrate that autoimmune disease does not quantitatively correlate with cancer immunity. Our approach may be generally applicable to the development of human therapeutic antibodies.

```
? b 410
       21sep07 10:29:00 User208760 Session D2891.1
            $0.51    0.145 DialUnits File1
     $0.51  Estimated cost File1
     $0.51  Estimated cost this search
     $0.51  Estimated total session cost   0.145 DialUnits

File 410:Dialog Comm.-of-Interest Newsletters 2007 /Feb
       (c) 2007 Dialog

      Set  Items  Description
      ---  -----  -----------
? set hi ;set hi
HILIGHT set on as ''
HILIGHT set on as ''
? begin 5,73,155,399
       21sep07 10:29:11 User208760 Session D2891.2
            $0.00    0.117 DialUnits File410
     $0.00  Estimated cost File410
     $0.03  TELNET
     $0.03  Estimated cost this search
     $0.54  Estimated total session cost   0.263 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R) 1926-2007/Sep W2
         (c) 2007 The Thomson Corporation
  File  73:EMBASE 1974-2007/Sep 21
         (c) 2007 Elsevier B.V.
  File 155:MEDLINE(R) 1950-2007/Sep 19
         (c) format only 2007 Dialog
  File 399:CA SEARCH(R) 1967-2007/UD=14713
         (c) 2007 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.

      Set  Items  Description
      ---  -----  -----------
? e au=gribben john ?

Ref   Items  Index-term
E1        1  AU=GRIBBEN JG J G
E2       27  AU=GRIBBEN JOHN
E3        0 *AU=GRIBBEN JOHN ?
E4      206  AU=GRIBBEN JOHN G
E5        1  AU=GRIBBEN K
E6        2  AU=GRIBBEN K.
E7        1  AU=GRIBBEN KATRINA
E8        1  AU=GRIBBEN KIRK
E9        4  AU=GRIBBEN M D
E10       1  AU=GRIBBEN M V
E11       3  AU=GRIBBEN M.D.
E12       1  AU=GRIBBEN M.V.

          Enter P or PAGE for more
? s e1-e4
              1  AU=GRIBBEN JG J G
             27  AU=GRIBBEN JOHN
              0  AU=GRIBBEN JOHN ?
            206  AU=GRIBBEN JOHN G
      S1    234  E1-E4
? s s1 and (anti(w)ctla?)
            234  S1
        1919702  ANTI
          11995  CTLA?
```

```
            763  ANTI(W)CTLA?
      S2      1  S1 AND (ANTI(W)CTLA?)
? t s2/3/all

 2/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2007 The Thomson Corporation. All rts. reserv.

17886854   BIOSIS NO.: 200400257611
Methods of inhibiting T cell proliferation or IL-2 accumulation with CTLA4-
  specific antibodies
AUTHOR: Gribben John G (Reprint); Freeman Gordon J; Nadler Lee M;
  Rennert Paul; Jellis Cindy L; Greenfield Edward; Gray Gary S
AUTHOR ADDRESS: Holliston, MA, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office
Patents  1281 (2): Apr. 13, 2004 2004
MEDIUM: e-file
PATENT NUMBER: US 6719972  PATENT DATE GRANTED: April 13, 2004 20040413
PATENT CLASSIFICATION: 424-1541  PATENT ASSIGNEE: Repligen Corporation,
Cambridge, MA, USA; Dana-Farber Cancer Institute  PATENT COUNTRY: USA
ISSN: 0098-1133 _(ISSN print)
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English
? s (anti(w)ctla?) and (autoimmun?)(10n)(treat? or therap? or inhibit? or suppress?
or prevent?)
Processing
Processing
Processing
         1919702  ANTI
           11995  CTLA?
             763  ANTI(W)CTLA?
          290906  AUTOIMMUN?
         8384681  TREAT?
         7825396  THERAP?
         5035017  INHIBIT?
         1050756  SUPPRESS?
         2756673  PREVENT?
           65759  AUTOIMMUN?(10N)((((TREAT? OR THERAP?) OR INHIBIT?) OR
                  SUPPRESS?) OR PREVENT?)
      S3     107  (ANTI(W)CTLA?) AND (AUTOIMMUN?)(10N)(TREAT? OR THERAP? OR
                  INHIBIT? OR SUPPRESS? OR PREVENT?)
? rd s3
      S4      63  RD S3  (unique items)
? t s4/3/all

 4/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2007 The Thomson Corporation. All rts. reserv.

0019791103   BIOSIS NO.: 200700450844
Inhibition of T cell activation and autoimmune diabetes using a
  B cell surface-linked CTLA-4 agonist
AUTHOR: Fife Brian T; Griffin Matthew D; Abbas Abul K; Locksley Richard M;
  Bluestone Jeffrey A (Reprint)
AUTHOR ADDRESS: Univ Calif San Francisco, Ctr Diabet, Dept Med, 513
  Parnassus Ave,Box 0540, San Francisco, CA 94143 USA**USA
AUTHOR E-MAIL ADDRESS: jbluest@diabetes.ucsf.edu
JOURNAL: Journal of Clinical Investigation  116 (8): p2252-2261 AUG 2006
2006
ISSN: 0021-9738
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
```

4/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0019614527 BIOSIS NO.: 200700274268
Autoimmunity correlates with tumor regression in patients with metastatic melanoma ***treated*** with ***anti*** - ***CTLA*** -4.
AUTHOR: Atria Peter (Reprint); Giao Phan Q; Michael Yellin J; Rosenberg Steven A
AUTHOR ADDRESS: Natl Canc Inst, Bethesda, MD USA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 46 (Suppl. S): p1455 APR 2005 2005
CONFERENCE/MEETING: 96th Annual Meeting of the American-Association-for-Cancer-Research Anaheim, CA, USA April 16 -20, 2005; 20050416
SPONSOR: Amer Assoc Canc Res
ISSN: 0197-016X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

4/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

19103713 BIOSIS NO.: 200600449108
Combination therapy with anti-CTL antigen-4 and anti-4-1BB antibodies enhances cancer immunity and reduces autoimmunity
AUTHOR: Kocak Ergun; Lute Kenneth; Chang Xing; May Kenneth F; Exten Katie R ; Zhang Huiming; Abdessalam Shahab F; Lehman Amy M; Jarjoura David; Zheng Pan; Liu Yang (Reprint)
AUTHOR ADDRESS: Univ Michigan, Med Ctr, Dept Surg, Div Immunotherapy,Program Mol Mech Dis and Canc Ctr, BSRB 1818,109 Zina Pitcher Pl, Ann Arbor, MI 48109 USA**USA
AUTHOR E-MAIL ADDRESS: yang1@umich.edu
JOURNAL: Cancer Research 66 (14): p7276-7284 JUL 15 2006 2006
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

19063818 BIOSIS NO.: 200600409213
Checkpoint blockade in cancer immunotherapy
BOOK TITLE: Advances in Immunology:CANCER IMMUNOTHERAPY
AUTHOR: Korman Alan J (Reprint); Peggs Karl S; Allison James P
BOOK AUTHOR/EDITOR: Allison JP (Editor); Franoff G (Editor)
AUTHOR ADDRESS: Medarex Inc, Milpitas, CA 95035 USA**USA
SERIES TITLE: ADVANCES IN IMMUNOLOGY 90 p297-339 2006
BOOK PUBLISHER: ELSEVIER ACADEMIC PRESS INC, 525 B STREET, SUITE 1900, SAN DIEGO, CA 92101-4495 USA
ISSN: 0065-2776 (print) ISBN: 0-12-022489-5 (H)
DOCUMENT TYPE: Book Chapter; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

4/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

19049079 BIOSIS NO.: 200600394474
Comment on "Analysis of the cellular mechanism of antitumor responses and autoimmunity in patients treated with CTLA-4 blockade"
AUTHOR: O'Mahony Deirdre (Reprint); Janik John E
AUTHOR ADDRESS: NCI, Metabol Branch, Bethesda, MD 20892 USA**USA
JOURNAL: Journal of Immunology 176 (9): p5136 MAY 1 2006 2006
ISSN: 0022-1767
DOCUMENT TYPE: Letter; Editorial
RECORD TYPE: Citation
LANGUAGE: English

4/3/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

19024616 BIOSIS NO.: 200600370011
Intrapatient dose escalation of anti-CTLA-4 antibody in patients with metastatic melanoma
AUTHOR: Maker Ajay V; Yang James C; Sherry Richard M; Topalian Suzanne L; Kannula Udai S; Royal Richard E; Hughes Marybeth; Yellin Michael J; Haworth Leah R; Levy Catherine; Allen Tamika; Mavroukakis Sharon A; Attia Peter; Rosenberg Steven A (Reprint)
AUTHOR ADDRESS: NCI, Surg Branch, NIH, CRC, Rm 3-3940,10 Ctr Dr,MSC 1201, Bethesda, MD 20814 USA**USA
AUTHOR E-MAIL ADDRESS: sar@nih.gov
JOURNAL: Journal of Immunotherapy 29 (4): p455-463 JUL-AUG 2006 2006
ISSN: 1524-9557
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

18863924 BIOSIS NO.: 200600209319
Regulation of murine chronic colitis by CD4+CD25-PD-1+ regulatory T cells
AUTHOR: Totsuka Teruji; Kanai Takanori; Makita Shin; Fujii Rei; Nemoto Yasuhiro; Watanabe Mamoru
JOURNAL: Gastroenterology 128 (4, Suppl. 2): pA56 APR 2005 2005
CONFERENCE/MEETING: Annual Meeting of the American-Gastroenterological-Association/Digestive-Disease-Week Chicago, IL, USA May 14 -19, 2005; 20050514
SPONSOR: Amer Gastroenterol Assoc
ISSN: 0016-5085
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

4/3/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

18761339 BIOSIS NO.: 200600106734
Analysis of the cellular mechanism of antitumor responses and autoimmunity in patients treated with CTLA-4 blockade
AUTHOR: Maker Ajay V; Attia Peter; Rosenberg Steven A (Reprint)

AUTHOR ADDRESS: NCI, Surg Branch, NIH, CRC Room 3-3888,10 Ctr Dr,MSC 1201, Bethesda, MD 20814 USA**USA
AUTHOR E-MAIL ADDRESS: sar@nih.gov
JOURNAL: Journal of Immunology 175 (11): p7746-7754 DEC 1 2005 2005
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

18540659 BIOSIS NO.: 200510235159
Regulation of murine chronic colitis by CD4(+)CD25(-) programmed death-1(+) T cells
AUTHOR: Totsuka Teruji; Kanai Takanori (Reprint); Makita Shin; Fujii Rei; Nemoto Yasuhiro; Oshima Shigeru; Okamoto Ryuichi; Koyanagi Akemi; Akiba Hisaya; Okumura Ko; Yagita Hideo; Watanabe Mamoru
AUTHOR ADDRESS: Tokyo Med and Dent Univ, Dept Gastroenterol and Hepatol, Grad Sch, Bunkyo Ku, 1-5-45 Yushima, Tokyo 1138519, Japan**Japan
AUTHOR E-MAIL ADDRESS: taka.gast@tmd.ac.jp
JOURNAL: European Journal of Immunology 35 (6): p1773-1785 JUN 2005 2005
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

18456536 BIOSIS NO.: 200510151036
Cytotoxic T lymphocyte-associated antigen 4 blockade in patients with metastatic melanoma - A new cause of uveitis
AUTHOR: Robinson Michael R (Reprint); Chan Chi-Chao; Yang James C; Rubin Benjamin I; Gracia Gerald J; Sen H Nida; Csaky Karl G; Rosenberg Steven A
AUTHOR ADDRESS: NEI, NIH, 10-10S229,10 Ctr Dr MSC 1863, Bethesda, MD 20892 USA**USA
AUTHOR E-MAIL ADDRESS: robinsonm@nei.nih.gov
JOURNAL: Journal of Immunotherapy 27 (6): p478-479 NOV-DEC04 2004
ISSN: 1524-9557
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

4/3/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

18045745 BIOSIS NO.: 200400416534
Targeted CTLA-4 engagement induces CD4+CD25+CTLA-4high T regulatory cells with target (allo)antigen specificity
AUTHOR: Vasu Chenthamarakshan; Prabhakar Bellur S; Holterman Mark J (Reprint)
AUTHOR ADDRESS: Coll MedDept Surg, Univ Illinois, 840 S Wood St,Mail Code 958, Chicago, IL, 60612, USA**USA
AUTHOR E-MAIL ADDRESS: rmasjet@uic.edu
JOURNAL: Journal of Immunology 173 (4): p2866-2876 August 15, 2004 2004
MEDIUM: print
ISSN: 0022-1767 _(ISSN print)

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

17658985 BIOSIS NO.: 200400029742
CD4+CD25+ regulatory T cells cure murine colitis: The role of IL-10, TGF-beta, and CTLA4.
AUTHOR: Liu Haiying; Hu Bin; Xu Damo (Reprint); Liew Foo Y (Reprint)
AUTHOR ADDRESS: Division of Immunology, Infection and Inflammation, University of Glasgow, Glasgow, G11 6NT, UK**UK
AUTHOR E-MAIL ADDRESS: d.xu@clinmed.gla.ac.uk; F.Y.Liew@clinmed.gla.ac.uk
JOURNAL: Journal of Immunology 171 (10): p5012-5017 November 15, 2003 2003
MEDIUM: print
ISSN: 0022-1767 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

17440741 BIOSIS NO.: 200300399171
Inhibitory signal override increases susceptibility to mercury-induced ***autoimmunity*** .
AUTHOR: Zheng Yan; Monestier Marc (Reprint)
AUTHOR ADDRESS: Department of Microbiology and Immunology, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA, 19140, USA**USA
AUTHOR E-MAIL ADDRESS: marcm@temple.edu
JOURNAL: Journal of Immunology 171 (3): p1596-1601 August 1, 2003 2003
MEDIUM: print
ISSN: 0022-1767 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

17297991 BIOSIS NO.: 200300256710
Targeted engagement of CTLA-4 ***prevents*** ***autoimmune*** thyroiditis.
AUTHOR: Vasu Chenthamarakshan; Gorla Seema R; Prabhakar Bellur S; Holterman Mark J (Reprint)
AUTHOR ADDRESS: Department of Surgery, University of Illinois at Chicago, Chicago, IL, 60612, USA**USA
AUTHOR E-MAIL ADDRESS: rmasjet@uic.edu
JOURNAL: International Immunology 15 (5): p641-654 May 2003 2003
MEDIUM: print
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/15 (Item 15 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

16777035 BIOSIS NO.: 200200370546
A functional link between CTLA-4 and cell surface associated TGF-beta in CD4+CD25+ suppressor T cell-mediated immunosuppression
AUTHOR: Chen Wanjun (Reprint); Sim Davis (Reprint); Jin Wenwen (Reprint); Kim Edward (Reprint); Hardegen Neil (Reprint); Bluestone Jeffrey A; Wahl Sharon M (Reprint)
AUTHOR ADDRESS: OIIB, NIDCR, 30, Convent Dr., Bethesda, MD, 20892, USA**USA
JOURNAL: FASEB Journal 16 (5): pA1056 March 22, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002; 20020420
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

4/3/16 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16775603 BIOSIS NO.: 200200369114
Anergy in peripheral memory CD4 T cells induced by low avidity engagement of T cell receptor
AUTHOR: Mirshahidi Saied (Reprint); Huang Ching-Tai; Sadegh-Nasseri Scheherazade (Reprint)
AUTHOR ADDRESS: Pathology, Johns Hopkins Medical Inst., 720 Rutland Ave, Ross 664-E, Baltimore, MD, 21205, USA**USA
JOURNAL: FASEB Journal 16 (4): pA714 March 20, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002; 20020420
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

4/3/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16680032 BIOSIS NO.: 200200273543
The role of CTLA-4 in induction and maintenance of peripheral T cell tolerance
AUTHOR: Eagar Todd N; Karandikar Nitin J; Bluestone Jeffrey A; Miller Stephen D (Reprint)
AUTHOR ADDRESS: Department of Microbiology-Immunology, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL, 60611, USA**USA
JOURNAL: European Journal of Immunology 32 (4): p972-981 April, 2002 2002
MEDIUM: print
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/18 (Item 18 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

16397083 BIOSIS NO.: 200100568922
Targeted delivery of anti-CTLA-4 antibody downregulates T cell function in vitro and in vivo
AUTHOR: Rao Seema; Vasu Chenthamarakshan; Martinez Osvaldo; Kaithamana Shashi; Prabhakar Bellur S; Holterman Mark J (Reprint)
AUTHOR ADDRESS: Division of Pediatric Surgery, Department of Surgery, College of Medicine, University of Illinois at Chicago, Chicago, IL, 60612, USA**USA
JOURNAL: Clinical Immunology (Orlando) 101 (2): p136-145 November, 2001 2001
MEDIUM: print
ISSN: 1521-6616
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16355481 BIOSIS NO.: 200100527320
Oral tolerance: Immune mechanisms and the generation of Th3-type TGF-beta-secreting regulatory cells
AUTHOR: Weiner Howard L (Reprint)
AUTHOR ADDRESS: Department of Neurology, Center for Neurologic Diseases, Harvard Medical School, Brigham and Women's Hospital, 77 Avenue Louis Pasteur, HIM 730, Boston, MA, 02115-5817, USA**USA
JOURNAL: Microbes and Infection 3 (11): p947-954 September, 2001 2001
MEDIUM: print
ISSN: 1286-4579
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

4/3/20 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16270278 BIOSIS NO.: 200100442117
Elucidating the autoimmune and antitumor effector mechanisms of a treatment based on cytotoxic T lymphocyte antigen-4 blockade in combination with a B16 melanoma vaccine: Comparison of prophylaxis and therapy
AUTHOR: van Elsas Andrea; Sutmuller Roger P M; Hurwitz Arthur A; Ziskin Jennifer; Villasenor Jennifer; Medema Jan-Paul; Overwijk Willem W; Restifo Nicholas P; Melief Cornelis J M; Offringa Rienk; Allison James P (Reprint)
AUTHOR ADDRESS: Cancer Research Lab, HHMI, 401 LSA UC Berkeley, Berkeley, CA, 94720, USA**USA
JOURNAL: Journal of Experimental Medicine 194 (4): p481-489 August 20, 2001 2001
MEDIUM: print
ISSN: 0022-1007
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/21 (Item 21 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

16213063 BIOSIS NO.: 200100384902
Adenovirus-mediated gene transfer of CTLA-4Ig fusion protein in the suppression of experimental autoimmune arthritis
AUTHOR: Quattrocchi Emilia; Dallman Margaret J; Feldmann Marc (Reprint)
AUTHOR ADDRESS: Kennedy Institute of Rheumatology, 1 Aspenlea Road, Hammersmith, London, W6 8LH, UK**UK
JOURNAL: Arthritis and Rheumatism 43 (8): p1688-1697 August, 2000 2000
MEDIUM: print
ISSN: 0004-3591
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16086708 BIOSIS NO.: 200100258547
Mechanism of CD4+CD25+ T cell immunoregulatory activity in vivo
AUTHOR: McHugh Rebecca S (Reprint); Thornton Angela (Reprint); Shevach Ethan M (Reprint)
AUTHOR ADDRESS: NIH, 9000 Rockville Pike, Bethesda, MD, 20892, USA**USA
JOURNAL: FASEB Journal 15 (5): pA1219 March 8, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001; 20010331
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

4/3/23 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16086688 BIOSIS NO.: 200100258527
Immunomodulation of experimental autoimmune thyroiditis using a bispecific antibody targeted to thyrotropin receptor and CTLA-4
AUTHOR: Chenthamarakshan V (Reprint); Rao S; Prabhakar B S; Holterman M J
AUTHOR ADDRESS: University of Illinois at Chicago, 835 S. Wolcott, Chicago, IL, 60612, USA**USA
JOURNAL: FASEB Journal 15 (5): pA1213 March 8, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001; 20010331
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

4/3/24 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

15870213 BIOSIS NO.: 200100042052
Therapy for autoimmune thyroiditis: Immunomodulation of

autoreactive T cells via CTLA4 signaling
AUTHOR: Rao S (Reprint); Chenthamarakshan V (Reprint); Martinez O (Reprint) ; Kaithamana S (Reprint); Prabhakar B S (Reprint); Holterman M J (Reprint)
AUTHOR ADDRESS: University of Illinois at Chicago, Chicago, IL, 60612, USA **USA
JOURNAL: FASEB Journal 14 (6): pA1079 April 20, 2000 2000
MEDIUM: print
CONFERENCE/MEETING: Joint Annual Meeting of the American Association of Immunologists and the Clinical Immunology Society Seattle, Washington, USA May 12-16, 2000; 20000512
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

4/3/25 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

15561659 BIOSIS NO.: 200000279972
The role of CTLA-4 in tolerance induction and T cell differentiation in experimental autoimmune encephalomyelitis: I.v. antigen administration
AUTHOR: Ratts Robert B; Arredondo LaChelle R; Bittner Patrice; Perrin Peter J; Lovett-Racke Amy E; Racke Michael K (Reprint)
AUTHOR ADDRESS: Department of Neurology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX, 75235-9036, USA** USA
JOURNAL: International Immunology 11 (12): p1889-1895 Dec., 1999 1999
MEDIUM: print
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/26 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

15561658 BIOSIS NO.: 200000279971
The role of CTLA-4 in tolerance induction and T cell differentiation in experimental autoimmune encephalomyelitis: I.p. Antigen administration
AUTHOR: Ratts Robert B; Arredondo LaChelle R; Bittner Patrice; Perrin Peter J; Lovett-Racke Amy E; Racke Michael K (Reprint)
AUTHOR ADDRESS: Department of Neurology, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX, 75235-9036, USA** USA
JOURNAL: International Immunology 11 (12): p1881-1888 Dec., 1999 1999
MEDIUM: print
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

4/3/27 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

14680045 EMBASE No: 2005527172
Tumor regression and autoimmunity in patients treated with cytotoxic T lymphocyte-associated antigen 4 blockade and interleukin 2: A

phase I/II study
Maker A.V.; Phan G.Q.; Attia P.; Yang J.C.; Sherry R.M.; Topalian S.L.; Kammula U.S.; Royal R.E.; Haworth L.R.; Levy C.; Kleiner D.; Mavroukakis S.A.; Yellin M.; Rosenberg S.A.
Dr. S.A. Rosenberg, Surgery Branch, National Cancer Institute, National Institutes of Health, 10 Center Drive, Bethesda, MD 20814 United States
AUTHOR EMAIL: sar@nih.gov
Annals of Surgical Oncology (ANN. SURG. ONCOL.) (United States) 2005, 12/12 (1005-1016)
CODEN: ASONF ISSN: 1068-9265 eISSN: 1534-4681
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 26

4/3/28 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

14679206 EMBASE No: 2005487280
Cytotoxic T-lymphocyte-associated antigen-4 blockage can induce autoimmune hypophysitis in patients with metastatic melanoma and renal cancer
Blansfield J.A.; Beck K.E.; Tran K.; Yang J.C.; Hughes M.S.; Kammula U.S.; Royal R.E.; Topalian S.L.; Haworth L.R.; Levy C.; Rosenberg S.A.; Sherry R.M.
R.M. Sherry, Surgery Branch, National Cancer Institute, National Institutes of Health CRC, 10 Center Drive, Bethesda, MD 20892-1201 United States
AUTHOR EMAIL: Richard Sherry@nih.gov
Journal of Immunotherapy (J. IMMUNOTHER.) (United States) 2005, 28/6 (593-598)
CODEN: JOIME ISSN: 1524-9557
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 16

4/3/29 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

14564444 EMBASE No: 2007323650
The combined activation of positive costimulatory signals with modulation of a negative costimulatory signal for the enhancement of vaccine-mediated T-cell responses
Chakraborty M.; Schlom J.; Hodge J.W.
J. Schlom, Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Institutes of Health, 10 Center Drive, Bethesda, MD 20892 United States
AUTHOR EMAIL: js141c@nih.gov
Cancer Immunology, Immunotherapy (CANCER IMMUNOL. IMMUNOTHER.) (Germany) 2007, 56/9 (1471-1484)
CODEN: CIIMD ISSN: 0340-7004
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 47

4/3/30 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

14552414 EMBASE No: 2007304418

CTLA-4 blockade in murine bone marrow chimeras induces a host-derived antileukemic effect without graft-versus-host disease
Fevery S.; Billiau A.D.; Sprangers B.; Rutgeerts O.; Lenaerts C.; Goebels J.; Landuyt W.; Kasran A.; Boon L.; Sagaert X.; De Wolf-Peeters C.; Waer M.; Vandenberghe P.
A.D. Billiau, Laboratory of Experimental Transplantation, University of Leuven, Leuven Belgium
Leukemia (LEUKEMIA) (United Kingdom) 2007, 21/7 (1451-1459)
CODEN: LEUKE ISSN: 0887-6924 eISSN: 1476-5551
PUBLISHER ITEM IDENTIFIER: 2404720
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 68

4/3/31 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

14546270 EMBASE No: 2007309838
Combination of tumor site-located CTL-associated antigen-4 blockade and systemic regulatory T-cell depletion induces tumor-destructive immune responses
Tuve S.; Chen B.-M.; Liu Y.; Cheng T.-L.; Toure P.; Sow P.S.; Feng Q.; Kiviat N.; Strauss R.; Ni S.; Li Z.-Y.; Roffler S.R.; Lieber A.
S.R. Roffler, Institute of Biomedical Sciences, Academia Sinica, Taipei 11529 Taiwan
AUTHOR EMAIL: sroff@ibms.sinica.edu.tw
Cancer Research (CANCER RES.) (United States) 15 JUN 2007, 67/12 (5929-5939)
CODEN: CNREA ISSN: 0008-5472
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

4/3/32 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

14529913 EMBASE No: 2007299355
A pilot trial of CTLA-4 blockade with human anti-CTLA-4 in patients with hormone-refractory prostate cancer
Small E.J.; Tchekmedyian N.S.; Rini B.I.; Fong L.; Lowy I.; Allison J.P.
E.J. Small, UCSF Comprehensive Cancer Center, University of California, San Francisco, 1600 Divisadero Street, San Francisco, CA 94115 United States
AUTHOR EMAIL: smalle@medicine.ucsf.edu
Clinical Cancer Research (CLIN. CANCER RES.) (United States) 15 MAR 2007, 13/6 (1810-1815)
CODEN: CCREF ISSN: 1078-0432
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 20

4/3/33 (Item 7 from file: 73).
DIALOG(R)File 73:EMBASE

14363492 EMBASE No: 2007112848
A pilot study of CTLA-4 blockade after cancer vaccine failure in patients with advanced malignancy
O'Mahony D.; Morris J.C.; Quinn C.; Gao W.; Wilson W.H.; Gause B.;

Pittaluga S.; Neelapu S.; Brown M.; Fleisher T.A.; Gulley J.L.; Schlom J.; Nussenblatt R.; Albert P.; Davis T.A.; Lowy I.; Petrus M.; Waldmann T.A.; Janik J.E.
J.E. Janik, Metabolism Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD 20892-1457 United States
AUTHOR EMAIL: janikj@mail.nih.gov
Clinical Cancer Research (CLIN. CANCER RES.) (United States) 01 FEB 2007, 13/3 (958-964)
CODEN: CCREF ISSN: 1078-0432
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 32

4/3/34 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

14330061 EMBASE No: 2007102132
Autoimmunity correlates with tumor regression in patients with metastatic melanoma treated with anti-cytotoxic T-lymphocyte antigen-4
Atria P.; Phan G.Q.; Maker A.V.; Robinson M.R.; Quezado M.M.; Yang J.C.; Sherry R.M.; Topalian S.L.; Kammula U.S.; Royal R.E.; Restifo N.P.; Haworth L.R.; Levy C.; Mavroukakis S.A.; Nichol G.; Yellin M.J.; Rosenberg S.A.
Dr. S.A. Rosenberg, Surgery Branch, National Cancer Institute, National Institutes of Health, 10 Center Dr, Bethesda, MD 20892-1201 United States
AUTHOR EMAIL: sar@nih.gov
Journal of Clinical Oncology (J. CLIN. ONCOL.) (United States) 2005, 23/25 (6043-6053)
CODEN: JCOND ISSN: 0732-183X
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 42

4/3/35 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

14312963 EMBASE No: 2007092561
Cancer vaccine under down-modulation of regulatory T cells
Yamaguchi Y.; Okita R.; Ohara M.; Ikeda T.; Okawaki M.; Nagamine I.; Hironaka K.; Emi A.; Hihara J.
Dr. Y. Yamaguchi, Department of Surgical Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8553 Japan
Biotherapy (BIOTHERAPY (JAPAN)) (Japan) 2007, 21/1 (42-47)
CODEN: BITPE ISSN: 0914-2223
DOCUMENT TYPE: Journal ; Article
LANGUAGE: JAPANESE SUMMARY LANGUAGE: ENGLISH; JAPANESE
NUMBER OF REFERENCES: 25

4/3/36 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

14285354 EMBASE No: 2007070545
Current topics in melanoma
Wolchok J.D.; Saenger Y.M.
J.D. Wolchok, Ludwig Center for Cancer Immunotherapy, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021

United States
AUTHOR EMAIL: wolchokj@mskcc.org
Current Opinion in Oncology (CURR. OPIN. ONCOL.) (United States) 2007
, 19/2 (116-120)
CODEN: CUOOE ISSN: 1040-8746
PUBLISHER ITEM IDENTIFIER: 00001622200703000000009
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
CLINICAL TRIALS NUMBER: NCT00297895--ClinicalTrials.gov
NUMBER OF REFERENCES: 38

4/3/37 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

13838855 EMBASE No: 2006235892
The immunotherapy potential of agonistic anti-CD137 (4-1BB) monoclonal antibodies for malignancies and chronic viral diseases
EL POTENCIAL DE LA INMUNOMODULACION CON ANTICUERPOS MONOCLONALES ANTI-CD137 (4-1BB) PARA TERAPIA DE ENFERMEDADES MALIGNAS E INFECCIONES VIRALES CRONICAS
Alfaro C.; Murillo O.; Tirapu I.; Azpilicueta A.; Huarte E.; Arina A.; Arribillaga L.; Perez-Gracia J.L.; Bendandi M.; Prieto J.; Lasarte J.J.; Melero I.
I. Melero, Area de Terapia Genica Y Hepatologia, Centro de Investigacion Medica Aplicada (CIMA), Avda. Pio XII, 55, 31008 Pamplona Spain
AUTHOR EMAIL: imelero@unav.es
Anales del Sistema Sanitario de Navarra (AN. SIST. SANIT. NAVARRA) (Spain) 2006, 29/1 (77-96)
CODEN: ASSNF ISSN: 1137-6627 eISSN: 1137-6627
DOCUMENT TYPE: Journal ; Review
LANGUAGE: SPANISH SUMMARY LANGUAGE: ENGLISH; SPANISH
NUMBER OF REFERENCES: 97

4/3/38 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

13794443 EMBASE No: 2006208185
Strategies for the development of more effective adjuvant therapy of melanoma: Current and future explorations of antibodies, cytokines, vaccines, and combinations
Kirkwood J.M.; Moschos S.; Wang W.
J.M. Kirkwood, University of Pittsburgh, School of Medicine, Hillman Cancer Research Pavilion, 5117 Centre Avenue, Pittsburgh, PA 15213-2584 United States
AUTHOR EMAIL: kirkwoodjm@upmc.edu
Clinical Cancer Research (CLIN. CANCER RES.) (United States) 01 APR 2006, 12/7 II (2331s-2336s)
CODEN: CCREF ISSN: 1078-0432
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 7

4/3/39 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

13427536 EMBASE No: 2005497259
Human CTLA4 knock-in mice unravel the quantitative link between tumor immunity and autoimmunity induced by anti-CTLA-4 antibodies

Lute K.D.; May Jr. K.F.; Lu P.; Zhang H.; Kocak E.; Mosinger B.; Wolford C.; Phillips G.; Caligiuri M.A.; Zheng P.; Liu Y.
Y. Liu, Department of Pathology, Ohio State University Medical Center, 129 Hamilton Hall, 1645 Neil Ave, Columbus, OH 43210 United States
AUTHOR EMAIL: liu-3@medctr.osu.edu
Blood (BLOOD) (United States) 2005, 106/9 (3127-3133)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

4/3/40 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

13211201 EMBASE No: 2005278804
Regulation of murine chronic colitis by CD4SUP+CD25SUP- programmed death-1SUP+ T cells
Totsuka T.; Kanai T.; Makita S.; Fujii R.; Nemoto Y.; Oshima S.; Okamoto R.; Koyanagi A.; Akiba H.; Okumura K.; Yagita H.; Watanabe M.
T. Kanai, Department of Gastroenterology and Hepatology, Graduate School, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519 Japan
AUTHOR EMAIL: taka.gast@tmd.ac.jp
European Journal of Immunology (EUR. J. IMMUNOL.) (Germany) 2005, 35/6 (1773-1785)
CODEN: EJIMA ISSN: 0014-2980
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 27

4/3/41 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

12758819 EMBASE No: 2004345090
Targeted CTLA-4 engagement induces CD4SUP+CD25SUP+CTLA- 4SUPhigh T regulatory cells with target (allo)antigen specificity
Vasu C.; Prabhakar B.S.; Holterman M.J.
Dr. M.J. Holterman, Department of Surgery, College of Medicine, University of Illinois, 840 South Wood Street, Chicago, IL 60612 United States
AUTHOR EMAIL: rmasjet@uic.edu
Journal of Immunology (J. IMMUNOL.) (United States) 15 AUG 2004, 173/4 (2866-2876)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 55

4/3/42 (Item 16 from file: 73)
DIALOG(R)File 73:EMBASE

12560360 EMBASE No: 2004156803
CTLA-4 blockade in combination with xenogeneic DNA vaccines enhances T-cell responses, tumor immunity and autoimmunity to self antigens in animal and cellular model systems
Gregor P.D.; Wolchok J.D.; Ferrone C.R.; Buchinshky H.; Guevara-Patin(tilde)o J.A.; Perales M.-A.; Mortazavi F.; Bacich D.; Heston W.; Latouche J.-B.; Sadelain M.; Allison J.P.; Scher H.I.; Houghton A.N.

P.D. Gregor, Mem. Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 United States
AUTHOR EMAIL: gregorp@mskcc.org
Vaccine (VACCINE) (United Kingdom) 16 APR 2004, 22/13-14 (1700-1708)
CODEN: VACCD ISSN: 0264-410X
PUBLISHER ITEM IDENTIFIER: S0264410X04000933
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 48

4/3/43 (Item 17 from file: 73)
DIALOG(R)File 73:EMBASE

12384948 EMBASE No: 2003474839
CD4SUP+CD25SUP+ Regulatory T Cells Cure Murine Colitis: The Role of IL-10, TGF-beta, and CTLA4
Liu H.; Hu B.; Xu D.; Liew F.Y.
F.Y. Liew, Div. Immunol., Infect./Inflammation, University of Glasgow, Glasgow, G11 6NT United Kingdom
AUTHOR EMAIL: F.Y.Liew@clinmed.gla.ac.uk
Journal of Immunology (J. IMMUNOL.) (United States) 15 NOV 2003, 171/10 (5012-5017)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 26

4/3/44 (Item 18 from file: 73)
DIALOG(R)File 73:EMBASE

12174978 EMBASE No: 2003286028
Cancer regression and autoimmunity induced by cytotoxic T lymphocyte-associated antigen 4 blockade in patients with metastatic melanoma
Phan G.Q.; Yang J.C.; Sherry R.M.; Hwu P.; Topalian S.L.; Schwartzentruber D.J.; Restifo N.P.; Haworth L.R.; Seipp C.A.; Freezer L.J.; Morton K.E.; Mavroukakis S.A.; Duray P.H.; Steinberg S.M.; Allison J.P.; Davis T.A.; Rosenberg S.A.
S.A. Rosenberg, Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892 United States
AUTHOR EMAIL: sar@nih.gov
Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 08 JUL 2003, 100/14 (8372-8377)
CODEN: PNASA ISSN: 0027-8424
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 37

4/3/45 (Item 19 from file: 73)
DIALOG(R)File 73:EMBASE

11359278 EMBASE No: 2001373634
Anergy in peripheral memory CD4SUP+ T cells induced by low avidity engagement of T cell receptor
Mirshahidi S.; Huang C.; Sadegh-Nasseri S.
S. Sadegh-Nasseri, Ross Bldg., 720 Rutland Ave., Baltimore, MD 21205 United States

AUTHOR EMAIL: ssadegh@jhmi.edu
Journal of Experimental Medicine (J. EXP. MED.) (United States) 17 SEP 2001, 194/6 (719-731)
CODEN: JEMEA ISSN: 0022-1007
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 77

4/3/46 (Item 20 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2007 Elsevier B.V. All rts. reserv.

10783480 EMBASE No: 2000264787
Activated Self-MHC-reactive T cells have the cytokine phenotype of Th3/T regulatory cell 1 T cells
Kitani A.; Chua K.; Nakamura K.; Strober W.
Dr. W. Strober, Mucosal Immunity Section, Laboratory of Clinical Investigation, Natl. Inst. of Allergy/Infect. Dis., Bethesda, MD 20852 United States
AUTHOR EMAIL: wstrober@niaid.nih.gov
Journal of Immunology (J. IMMUNOL.) (United States) 15 JUL 2000, 165/2 (691-702)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 44

4/3/47 (Item 21 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2007 Elsevier B.V. All rts. reserv.

10716084 EMBASE No: 2000200495
Novel approaches to therapy for systemic lupus erythematosus
Zandman-Goddard G.; Shoenfeld Y.
Y. Shoenfeld, Department of Medicine B, Sheba Medical Center, Tel Hashomer 52621 Israel
AUTHOR EMAIL: shoenfel@post.tau.ac.il
European Journal of Internal Medicine (EUR. J. INTERN. MED.) (Netherlands) 2000, 11/3 (130-134)
CODEN: EJIME ISSN: 0953-6205
PUBLISHER ITEM IDENTIFIER: S0953620500000741
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 29

4/3/48 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2007 Dialog. All rts. reserv.

16086264 PMID: 16670731
[The immunotherapy potential of agonistic anti-CD137 (4-1BB) monoclonal antibodies for malignancies and chronic viral diseases]
El potencial de la inmunomodulacion con anticuerpos monoclonales anti-CD137 (4-1BB) para terapia de enfermedades malignas e infecciones virales cronicas.
Alfaro C; Murillo O; Tirapu I; Azpilicueta A; Huarte E; Arina A; Arribillaga L; Perez-Gracia J L; Bendandi M; Prieto J; Lasarte J J; Melero I
Area de Terapia Genica y Hepatologia, Centro de Investigacion Medica Aplicada, Pamplona.
Anales del sistema sanitario de Navarra (Spain) Jan-Apr 2006, 29 (1)

p77-96, ISSN 1137-6627--Print Journal Code: 9710381
Publishing Model Print
Document type: Comparative Study; English Abstract; Journal Article; Review
Languages: SPANISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

4/3/49 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15840689 PMID: 16204013
Antitumor activity in melanoma and anti-self responses in a phase I trial with the anti-cytotoxic T lymphocyte-associated antigen 4 monoclonal antibody CP-675,206.
Ribas Antoni; Camacho Luis H; Lopez-Berestein Gabriel; Pavlov Dmitri; Bulanhagui Cecile A; Millham Robert; Comin-Anduix Begona; Reuben James M; Seja Elisabeth; Parker Charla A; Sharma Amarnath; Glaspy John A; Gomez-Navarro Jesus
Department of Medicine, Division of Hematology/Oncology Surgery, University of California at Los Angeles, CA, USA.
Journal of clinical oncology - official journal of the American Society of Clinical Oncology (United States) Dec 10 2005, 23 (35) p8968-77, ISSN 0732-183X--Print Journal Code: 8309333
Publishing Model Print-Electronic; Comment in J Clin Oncol. 2005 Dec 10;23(35) 8926-8; Comment in PMID 16204008
Document type: Clinical Trial, Phase I; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

4/3/50 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15682682 PMID: 16087944
Autoimmunity correlates with tumor regression in patients with metastatic melanoma treated with anti-cytotoxic T-lymphocyte antigen-4.
Attia Peter; Phan Giao Q; Maker Ajay V; Robinson Michael R; Quezado Martha M; Yang James C; Sherry Richard M; Topalian Suzanne L; Kammula Udai S; Royal Richard E; Restifo Nicholas P; Haworth Leah R; Levy Catherine; Mavroukakis Sharon A; Nichol Geoff; Yellin Michael J; Rosenberg Steven A
Surgery Branch, National Cancer Institute, National Institutes of Health, CRC, Room 3W-3940, 10 Center Dr, Bethesda, MD 20892-1201, USA.
Journal of clinical oncology - official journal of the American Society of Clinical Oncology (United States) Sep 1 2005, 23 (25) p6043-53, ISSN 0732-183X--Print Journal Code: 8309333
Contract/Grant No.: Z01 SC003811-31; SC; NCI
Publishing Model Print-Electronic; Comment in J Clin Oncol. 2005 Sep 1;23(25) 5875-7; Comment in PMID 16087939
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

4/3/51 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15341978 PMID: 15613700
Autoimmunity in a phase I trial of a fully human anti-cytotoxic T-lymphocyte antigen-4 monoclonal antibody with multiple melanoma peptides and Montanide ISA 51 for patients with resected stages III and IV melanoma.
Sanderson Kristin; Scotland Ronald; Lee Peter; Liu Dongxin; Groshen Susan ; Snively Jolie; Sian Shirley; Nichol Geoffrey; Davis Thomas; Keler Tibor; Yellin Michael; Weber Jeffrey
Department of Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA.
Journal of clinical oncology - official journal of the American Society of Clinical Oncology (United States) Feb 1 2005, 23 (4) p741-50, ISSN 0732-183X--Print Journal Code: 8309333
Publishing Model Print-Electronic; Comment in J Clin Oncol. 2005 Feb 1;23(4) 662-4; Comment in PMID 15613692
Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

4/3/52 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14583515 PMID: 14609212
The role of CD28 and CTLA4 in the function and homeostasis of CD4+CD25+ regulatory T cells.
Boden Elisa; Tang Qizhi; Bour-Jordan Helene; Bluestone Jeffrey A
UCSF Diabetes Center, University of California, San Francisco, 513 Parnassus Avenue, Box 0540, HSW Room 1114, San Francisco, CA 94143-0540, USA.
Novartis Foundation symposium (England) 2003, 252 p55-63; discussion 63-6, 106-14, ISSN 1528-2511--Print Journal Code: 9807767
Contract/Grant No.: F32 AI 10360; AI; NIAID
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

4/3/53 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13420254 PMID: 11591746
Activation of CD25(+)CD4(+) regulatory T cells by oral antigen administration.
Zhang X; Izikson L; Liu L; Weiner H L
Center for Neurologic Diseases, Harvard Medical School, Boston, MA 02115, USA.
Journal of immunology (Baltimore, Md. - 1950) (United States) Oct 15 2001, 167 (8) p4245-53, ISSN 0022-1767--Print Journal Code: 2985117R
Contract/Grant No.: AI43458; AI; NIAID; N538037; PHS
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

4/3/54 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

12179813 PMID: 10590254
The role of CTLA-4 in tolerance induction and ttigen administration cell differentiation in experimental autoimmune encephalomyelitis: i. v. antigen administration.
Ratts R B; Arredondo L R; Bittner P; Perrin P J; Lovett-Racke A E; Racke M K
Department of Neurology, Washington University School of Medicine, St Louis, MO 63110, USA.
International immunology (ENGLAND) Dec 1999, 11 (12) p1889-96, ISSN 0953-8178--Print Journal Code: 8916182
Contract/Grant No.: R01-NS-37513; NS; NINDS; R29-AI-43296; AI; NIAID
Publishing Model Print
Document type: Journal Article; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

4/3/55 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

146245513 CA: 146(13)245513f PATENT
Recombinant immunotoxin containing human perforin peptide p34 and humanized single-stranded antibody against CTL-4 antigen
INVENTOR(AUTHOR): Lu, Xiaofeng; Cheng, Jingqiu; Zeng, Lingyu; Wan, Lin; Qiu, Xiaoqing; Lu, Yanrong; Li, Shengfu; Chen, Lihong; Li, Youping; Bu, Hong
LOCATION: Peop. Rep. China,
ASSIGNEE: West China Hospital, Sichuan University
PATENT: Faming Zh. Sh. Gong. Shuom ; CN 1900117 A DATE: 20070124
APPLICATION: CN 10084311 (20050718)
PAGES: 28pp. CODEN: CNXXEV LANGUAGE: Chinese
PATENT CLASSIFICATIONS:

IPCR/8 + Level	Value	Position	Status	Version	Action	Source	Office:
C07K-0019/00	A	I	F	B 20060101		H	CN
C12N-0015/62	A	I	L	B 20060101		H	CN
C12N-0015/63	A	I	L	B 20060101		H	CN
A61K-0039/395	A	I	L	B 20060101		H	CN
A61P-0037/06	A	I	L	B 20060101		H	CN
A61P-0035/00	A	I	L	B 20060101		H	CN

4/3/56 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

146227669 CA: 146(12)227669g PATENT
Primatized monoclonal anti-human CD80 antibodies incapable of blocking CD80 binding to CTLA-4 for treating intestinal inflammation, autoimmune disease and organ rejection
INVENTOR(AUTHOR): Anderson, Darrell R.; Hanna, Nabil; Brams, Peter
LOCATION: USA
ASSIGNEE: Biogen Idec Inc.
PATENT: United States ; US 7175847 B1 DATE: 20070213
APPLICATION: US 2000576424 (20000522) *US 487550 (19950607) *US 746361 (19961108)
PAGES: 56pp., Cont.-in-part of U.S. Ser. No. 746,361, abandoned. CODEN: USXXAM LANGUAGE: English
PATENT CLASSIFICATIONS:

CLASS: 424153100; A61K-039/395A; C07K-016/28B

4/3/57 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

145102145 CA: 145(6)102145f PATENT
Anti-CD40 monoclonal antibodies antagonize C4BP-induced signaling
INVENTOR(AUTHOR): Luqman, Mohammad
LOCATION: USA
ASSIGNEE: Chiron Corporation
PATENT: PCT International ; WO 200673443 A2 DATE: 20060713
APPLICATION: WO 2005US14359 (20050427) *US 2004PV565775 (20040427)
PAGES: 97 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
IPCR/8 + Level Value Position Status Version Action Source Office:
A61P-0035/02 A I F B 20060101 H EP
A61K-0039/395 A I L B 20060101 H EP
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BW; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NA; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; SM; SY; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW DESIGNATED REGIONAL: AT; BE; BG; CH; CY ; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IS; IT; LT; LU; MC; NL; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

4/3/58 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

145025740 CA: 145(2)25740s JOURNAL
CTLA-4 blockade: Autoimmunity as treatment
AUTHOR(S): Kapadia, Dilnawaz; Fong, Lawrence
LOCATION: Department of Medicine, Division of Hematology and Oncology, University of California, San Francisco, San Francisco, CA, USA
JOURNAL: J. Clin. Oncol. (Journal of Clinical Oncology) DATE: 2005
VOLUME: 23 NUMBER: 35 PAGES: 8926-8928 CODEN: JCONDN ISSN: 0732-183X
LANGUAGE: English PUBLISHER: American Society of Clinical Oncology

4/3/59 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

144291290 CA: 144(16)291290n PATENT
Cancer combination therapy with anti-CTLA4 and anti-4-1BB antibodies
INVENTOR(AUTHOR): Liu, Yang; Zheng, Pan; Kocak, Ergun
LOCATION: USA
ASSIGNEE: Ohio State University Research Foundation
PATENT: PCT International ; WO 200629220 A2 DATE: 20060316
APPLICATION: WO 2005US31899 (20050907) *US 2004PV608000 (20040908)
PAGES: 38 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
IPCR/8 + Level Value Position Status Version Action Source Office:
A61K-0039/395 A I F B 20060101 H US
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BW; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NA; NG; NI; NO; NZ; OM; PG;

PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; SM; SY; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW DESIGNATED REGIONAL: AT; BE; BG; CH ; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IS; IT; LT; LU; LV; MC; NL; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

4/3/60 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

144267321 CA: 144(15)267321c PATENT
Assessment of CTLA-4 polymorphisms in CTLA-4 blockade immunotherapy and selecting a treatment regimen using the same
INVENTOR(AUTHOR): Nichol, Geoffrey M.; Yellin, Michael J.; Fischkoff, Steven; Weber, Jeffrey
LOCATION: USA
ASSIGNEE: Medarex Inc.
PATENT: PCT International ; WO 200628999 A2 DATE: 20060316
APPLICATION: WO 2005US31379 (20050901) *US 2004PV607225 (20040903) *US 2004PV611831 (20040920)
PAGES: 44 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
IPCR/8 + Level Value Position Status Version Action Source Office:
C12Q-0001/68 A I F B 20060101 H US
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BW; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NA; NG; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; SM; SY; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW DESIGNATED REGIONAL: AT; BE; BG; CH ; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IS; IT; LT; LU; LV; MC; NL; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

4/3/61 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

142022306 CA: 142(2)22306g PATENT
Therapeutic endpoint for anti-CTLA4 immunotherapy of cancer
INVENTOR(AUTHOR): Lowy, Israel; Nichol, Geoffrey M.
LOCATION: USA
ASSIGNEE: Medarex, Inc.
PATENT: U.S. Pat. Appl. Publ. ; US 20040241169 A1 DATE: 20041202
APPLICATION: US 2004857749 (20040527) *US 2003PV475067 (20030530)
PAGES: 16 pp. CODEN: USXXCO LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: 424155100; G01N-033/574A; A61K-039/395B

4/3/62 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

139336923 CA: 139(22)336923m PATENT
Anti-CTLA-4 antibodies for potentiating secondary immune response to antigen and for treating cancer, infection and autoimmune disease
INVENTOR(AUTHOR): Davis, Thomas; Keler, Tibor; Graziano, Robert; Korman, Alan J.
LOCATION: USA

ASSIGNEE: Medarex, Inc.
PATENT: PCT International ; WO 200386459 A1 DATE: 20031023
APPLICATION: WO 2003US11444 (20030411) *US PV372284 (20020412) *US PV381274 (20020517)
PAGES: 51 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: A61K-039/395A; A61K-038/16B; C07K-014/705B; C07K-016/28B
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SC; SD; SE; SG; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IT; LU; MC; NL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

4/3/63 (Item 9 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124229989 CA: 124(17)229989f PATENT
Ligands for induction of antigen specific apoptosis in T cells
INVENTOR(AUTHOR): Gribben, John G.; Freeman, Gordon J.; Nadler, Lee M.; Rennert, Paul; Jellis, Cindy L.; Greenfield, Edward; Gray, Gary S.
LOCATION: USA
ASSIGNEE: Repligen Corp.; Dana Farber Cancer Institute
PATENT: PCT International ; WO 9533770 A1 DATE: 951214
APPLICATION: WO 95US6726 (950602) *US 253783 (940603)
PAGES: 86 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: C07K-014/705A; C07K-016/28B; A61K-039/395B; A61K-038/17B
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
?

4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0019791103 BIOSIS NO.: 200700450844
Inhibition of T cell activation and autoimmune diabetes using a B cell surface-linked CTLA-4 agonist
AUTHOR: Fife Brian T; Griffin Matthew D; Abbas Abul K; Locksley Richard M; Bluestone Jeffrey A (Reprint)
AUTHOR ADDRESS: Univ Calif San Francisco, Ctr Diabet, Dept Med, 513 Parnassus Ave,Box 0540, San Francisco, CA 94143 USA**USA
AUTHOR E-MAIL ADDRESS: jbluest@diabetes.ucsf.edu
JOURNAL: Journal of Clinical Investigation 116 (8): p2252-2261 AUG 2006 2006
ISSN: 0021-9738
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CTL-associated antigen 4 (CTLA-4) engagement negatively regulates T cell activation and function and promotes immune tolerance. However, it has been difficult to explore the biology of selective engagement of CTLA-4 in vivo because CTLA-4 shares its ligands, B7-1 and B7-2, with CD28. To address this issue, we developed a Tg mouse expressing a single-chain, membrane-bound anti-CTLA-4 Ab (scFv) on B cells. B and T cells developed normally and exhibited normal phenotype in the steady state and after activation in these mice. However, B cells from scFv Tg(+) mice (scaCTLA4(+)) prevented T cell proliferation and cytokine production in mixed lymphocyte reactions. Additionally, mice treated with scaCTLA4+ B cells had decreased T cell-dependent B cell Ab production and class switching in vivo after antigen challenge. Furthermore, expression of this CTLA-4 agonist protected NOD mice from spontaneous ***autoimmune*** diabetes. Finally, this disease ***prevention*** occurred in Treg-deficient NOD.B7-1/B7-2 double-knockout mice, suggesting that the effect of the CTLA-4 agonist directly attenuates autoreactive T cell activation, not Treg activation. Together, results from this study demonstrate that selective ligation of CTLA-4 attenuates in vivo T cell responses, prevents development of autoimmunity, and represents a novel immunotherapeutic approach for the induction and maintenance of peripheral tolerance.

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0019614527 BIOSIS NO.: 200700274268
Autoimmunity correlates with tumor regression in patients with metastatic melanoma ***treated*** with ***anti*** - ***CTLA*** -4.
AUTHOR: Atria Peter (Reprint); Giao Phan Q; Michael Yellin J; Rosenberg Steven A
AUTHOR ADDRESS: Natl Canc Inst, Bethesda, MD USA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 46 (Suppl. S): p1455 APR 2005 2005
CONFERENCE/MEETING: 96th Annual Meeting of the American-Association-for-Cancer-Research Anaheim, CA, USA April 16 -20, 2005; 20050416
SPONSOR: Amer Assoc Canc Res
ISSN: 0197-016X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

4/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

17297991 BIOSIS NO.: 200300256710
Targeted engagement of CTLA-4 ***prevents*** ***autoimmune*** thyroiditis.
AUTHOR: Vasu Chenthamarakshan; Gorla Seema R; Prabhakar Bellur S; Holterman Mark J (Reprint)
AUTHOR ADDRESS: Department of Surgery, University of Illinois at Chicago, Chicago, IL, 60612, USA**USA
AUTHOR E-MAIL ADDRESS: rmasjet@uic.edu
JOURNAL: International Immunology 15 (5): p641-654 May 2003 2003
MEDIUM: print
ISSN: 0953-8178
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The CTLA-4-mediated signal is a critical step in the down-modulation of immune responses. The therapeutic potential of this signal to induce tissue-specific tolerance was investigated by using an anti-CTLA-4 antibody that was coupled to an antibody specific for the thyrotropin receptor. After in vivo administration, this bispecific antibody (BiAb) accumulated in the thyroid and prevented development of experimental autoimmune thyroiditis (EAT) in mice immunized with mouse thyroglobulin (mTg). Lymphocytes from BiAb-treated mice showed a significant reduction in their ability to proliferate, and to produce IL-2, IFN-gamma and tumor necrosis factor (TNF)-alpha, in response to mTg re-stimulation compared to lymphocytes from untreated mice. Moreover, BiAb-treated mice showed suppressed anti-mTg antibody response, lymphocytic infiltration of the thyroid and follicular destruction. The BiAb targeted to the thyroid most likely facilitated engagement of CTLA-4, resulting in an increase in the number of CD4+CD25+ T cells. These regulatory T cells suppressed in vitro mTg-specific T cell responses, which were associated with an enhanced transforming growth factor (TGF)-beta1 production. Neutralization of TGF-beta1 increased mTg-specific in vitro proliferation of, and IL-2 production by, T cells from BiAb-treated mice. Our data suggest that engagement of CTLA-4 expressed on activated autoreactive T cells in close proximity to the thyroid can increase the number of regulatory T cells and their ability to produce TGF-beta1, with a concomitant reduction in IFN-gamma and TNF-alpha, resulting in suppression of EAT.

4/7/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16680032 BIOSIS NO.: 200200273543
The role of CTLA-4 in induction and maintenance of peripheral T cell tolerance
AUTHOR: Eagar Todd N; Karandikar Nitin J; Bluestone Jeffrey A; Miller Stephen D (Reprint)
AUTHOR ADDRESS: Department of Microbiology-Immunology, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL, 60611, USA**USA
JOURNAL: European Journal of Immunology 32 (4): p972-981 April, 2002 2002
MEDIUM: print
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: T cell receptor engagement and the B7-CD28/CTLA-4 signaling pathways play critical roles in T cell activation and regulation. CD28 engagement results in T cell activation, differentiation and survival while CTLA-4 signals block IL-2 production, cell cycle progression and T cell differentiation. We explored the role of CTLA-4 in peripheral tolerance induced by intravenous administration of ethylene carbodiimide-fixed, antigen-coupled splenocytes in the PLP139-151-induced relapsing experimental autoimmune encephalomyelitis system. Tolerance induction with PLP139-151-coupled splenocytes correlates with low B7 expression on the fixed antigen-presenting cells, conditions that would favor CTLA-4-mediated inhibition. Administration of CTLA-4Ig or anti-CTLA-4 concomitant with the 'tolerogenic' stimulus, however, failed to reverse tolerance induction. In contrast, blocking CTLA-4 at the time of secondary 'immunogenic' encounter with antigen reversed the tolerant state. These findings indicate that CTLA-4 is required to maintain the unresponsive state of the tolerized T cells upon antigenic stimulation under inflammatory conditions and, therefore, have important implications for therapeutic regulation of ***autoimmune*** disease.

4/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16397083 BIOSIS NO.: 200100568922
Targeted delivery of anti-CTLA-4 antibody downregulates T cell function in vitro and in vivo
AUTHOR: Rao Seema; Vasu Chenthamarakshan; Martinez Osvaldo; Kaithamana Shashi; Prabhakar Bellur S; Holterman Mark J (Reprint)
AUTHOR ADDRESS: Division of Pediatric Surgery, Department of Surgery, College of Medicine, University of Illinois at Chicago, Chicago, IL, 60612, USA**USA
JOURNAL: Clinical Immunology (Orlando) 101 (2): p136-145 November, 2001 2001
MEDIUM: print
ISSN: 1521-6616
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: CTLA-4 is a T cell surface molecule that binds to the costimulatory molecules CD80 and CD86 on antigen-presenting cells and downregulates T cell function. Therefore, we wanted to test whether antigen-specific activated T cells could be inhibited through directed CTLA-4 signaling using a bispecific antibody (BiAb) capable of simultaneously binding to CTLA-4 and a tissue-specific antigen. The BiAb was prepared by linking two separate monoclonal antibodies against CTLA-4 and the thyroid-stimulating hormone receptor (TSHR). The mouse B cell lymphoma line M12 (H2d) was used to induce alloreactive T cells in CBA/J mice (H2k); M12 cells stably transfected with the cDNA encoding murine TSHR (mM12) were used to restimulate the alloresponse in vitro. Results of assays for in vitro T cell proliferation, IL-2 production, and cytotoxicity in the presence of BiAb demonstrated that the BiAb could inhibit the T cell alloresponse when stimulated with mM12 cells but not with M12 cells. This effect was dependent on binding of TSHR-bound BiAb to CTLA-4, since the addition of soluble CTLA-4-Ig blocked the inhibitory effect. Injection of mM12 cells, along with the BiAb, not with antibodies against TSHR or CTLA-4 either separately or together, into CBA/J mice (H2k) downregulated alloreactive T cell responses. Our study demonstrated that the presence of CTLA-4 signaling molecules on the surface of target cells can protect those cells from immune attack by antigen-specific T cells and suggested that a similar approach could have potential therapeutic value in transplant rejection and tissue-specific

autoimmune diseases.

4/7/24 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

15870213 BIOSIS NO.: 200100042052
Therapy for autoimmune thyroiditis: Immunomodulation of autoreactive T cells via CTLA4 signaling
AUTHOR: Rao S (Reprint); Chenthamarakshan V (Reprint); Martinez O (Reprint); Kaithamana S (Reprint); Prabhakar B S (Reprint); Holterman M J (Reprint)
AUTHOR ADDRESS: University of Illinois at Chicago, Chicago, IL, 60612, USA **USA
JOURNAL: FASEB Journal 14 (6): pA1079 April 20, 2000 2000
MEDIUM: print
CONFERENCE/MEETING: Joint Annual Meeting of the American Association of Immunologists and the Clinical Immunology Society Seattle, Washington, USA May 12-16, 2000; 20000512
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

4/7/39 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

13427536 EMBASE No: 2005497259
Human CTLA4 knock-in mice unravel the quantitative link between tumor immunity and autoimmunity induced by anti-CTLA-4 antibodies
Lute K.D.; May Jr. K.F.; Lu P.; Zhang H.; Kocak E.; Mosinger B.; Wolford C.; Phillips G.; Caligiuri M.A.; Zheng P.; Liu Y.
Y. Liu, Department of Pathology, Ohio State University Medical Center, 129 Hamilton Hall, 1645 Neil Ave, Columbus, OH 43210 United States
AUTHOR EMAIL: liu-3@medctr.osu.edu
Blood (BLOOD) (United States) 2005, 106/9 (3127-3133)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

Although results from preclinical studies in animal models have proven the concept for use of anti-cytotoxic T-lymphocyte antigen 4 (CTLA-4) antibodies in cancer immunotherapy, 2 major obstacles have hindered their successful application for human cancer therapy. First, the lack of in vitro correlates of the antitumor effect of the antibodies makes it difficult to screen for the most efficacious antibody by in vitro analysis. Second, significant autoimmune side effects have been observed in a recent clinical trial. In order to address these 2 issues, we have generated human CTLA4 gene knock-in mice and used them to compare a panel of anti-human CTLA-4 antibodies for their ability to induce tumor rejection and autoimmunity. Surprisingly, while all antibodies induced protection against cancer and demonstrated some autoimmune side effects, the antibody that induced the strongest protection also induced the least autoimmune side effects. These results demonstrate that autoimmune disease does not quantitatively correlate with cancer immunity. Our approach may be generally applicable to the development of human therapeutic antibodies.

?

```
 s (ctla?)(10n)(antibod? or immunoglobulin?)(10n)(apopto?)
          11995  CTLA?
        2253843  ANTIBOD?
         838986  IMMUNOGLOBULIN?
         553520  APOPTO?
      S5      41  (CTLA?)(10N)(ANTIBOD? OR IMMUNOGLOBULIN?)(10N)(APOPTO?)
? rd s5
      S6      24  RD S5  (unique items)
? t s6/3/all

 6/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2007 The Thomson Corporation. All rts. reserv.

0019519485   BIOSIS NO.: 200700179226
The role of Foxp3(+) regulatory T cells in liver transplant tolerance
AUTHOR: Li W (Reprint); Carper K; Zheng X X; Kuhr C S; Reyes J D; Liang Y;
  Perkins D L; Thomson A W; Perkins J D
AUTHOR ADDRESS: Univ Washington, Med Ctr, Dept Surg, Div Transplantat, Box
  356174,1959 NE Pacific St, Seattle, WA 98195 USA**USA
AUTHOR E-MAIL ADDRESS: weili8@u.washington.edu
JOURNAL: Transplantation Proceedings  38 (10, Sp. Iss. SI): p3205-3206 DEC
2006 2006
ISSN: 0041-1345
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English


 6/3/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2007 The Thomson Corporation. All rts. reserv.

18690257   BIOSIS NO.: 200600035652
CTLA-4 is constitutively expressed on tumor cells and can trigger apoptosis
  upon ligand interaction
AUTHOR: Contardi Elisabetta; Palmisano Giulio L; Tazzari Pier Luigi;
  Martelli Alberto M; Fala Federica; Fabbi Marina; Kato Tomohiro; Lucarelli
  Enrico; Donati Davide; Polito Letizia; Bolognesi Andrea; Ricci Francesca;
  Salvi Sandra; Gargaglione Vittoria; Mantero Stefano; Alberghini Marco;
  Ferrara Giovanni Battista; Pistillo Maria Pia (Reprint)
AUTHOR ADDRESS: Natl Inst Canc Res, Lab Translat Res A, Largo R Benzi 10,
  I-16132 Genoa, Italy**Italy
AUTHOR E-MAIL ADDRESS: mariapia.pistillo@istge.it
JOURNAL: International Journal of Cancer  117 (4): p538-550 NOV 20 2005
2005
ISSN: 0020-7136
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English


 6/3/3     (Item 3 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2007 The Thomson Corporation. All rts. reserv.

17886854   BIOSIS NO.: 200400257611
Methods of inhibiting T cell proliferation or IL-2 accumulation with CTLA4-
  specific antibodies
AUTHOR: Gribben John G (Reprint); Freeman Gordon J; Nadler Lee M; Rennert
  Paul; Jellis Cindy L; Greenfield Edward; Gray Gary S
AUTHOR ADDRESS: Holliston, MA, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office
Patents  1281 (2): Apr. 13, 2004 2004
```

MEDIUM: e-file
PATENT NUMBER: US 6719972 PATENT DATE GRANTED: April 13, 2004 20040413
PATENT CLASSIFICATION: 424-1541 PATENT ASSIGNEE: Repligen Corporation, Cambridge, MA, USA; Dana-Farber Cancer Institute PATENT COUNTRY: USA
ISSN: 0098-1133 _(ISSN print)
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

6/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

17337882 BIOSIS NO.: 200300295701
CTLA-4-FasL interferes with T cell activation and induces apoptosis.
AUTHOR: Huang Jui-Han (Reprint); Elhalel Michal Dranitzki; Schmidt William; Tykocinski Mark L
AUTHOR ADDRESS: Pathology and Laboratory Medicine, Univeristy of Pennsylvania, 422 Curie Blvd, Philadelphia, PA, 19104, USA**USA
AUTHOR E-MAIL ADDRESS: hhuang@mail.med.upenn.edu; michalelhalel@hotmail.com ; wschmidt@mail.med.upenn.edu; mlt4@mail.med.upenn.edu
JOURNAL: FASEB Journal 17 (4-5): pAbstract No. 414.1 March 2003 2003
MEDIUM: e-file
CONFERENCE/MEETING: FASEB Meeting on Experimental Biology: Translating the Genome San Diego, CA, USA April 11-15, 2003; 20030411
SPONSOR: FASEB
ISSN: 0892-6638 _(ISSN print)
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

6/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16576491 BIOSIS NO.: 200200170002
The CD154-CD40 costimulatory pathway in transplantation
AUTHOR: Yamada Akira; Sayegh Mohamed H (Reprint)
AUTHOR ADDRESS: Brigham and Women's Hospital, 75 Francis Street, Boston, MA, 02115, USA**USA
JOURNAL: Transplantation (Baltimore) 73 (1 Supplement): pS36-S39 January 15, 2002 2002
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

6/3/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16576466 BIOSIS NO.: 200200169977
Dendritic cells and second signal blockade: A step toward allograft tolerance?
AUTHOR: Rifle Gerard (Reprint); Mousson Christiane
AUTHOR ADDRESS: Department of Nephrology-Intensive Care-Transplantation, Hopital du Bocage, 2, Boulevard de Lattre de Tassigny, 21034, Dijon, France**France
JOURNAL: Transplantation (Baltimore) 73 (1 Supplement): pS1-S2 January 15, 2002 2002

MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

6/3/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

16133676 BIOSIS NO.: 200100305515
Patients with neoplastic and nonneoplastic hematologic diseases acquire CTLA-4 antibodies after blood transfusion
AUTHOR: Pistillo Maria Pia (Reprint); Tazzari Pier Luigi; Gaudiano Carlo; Cilla Vito; Kato Tomohiro; Matsui Toshihiro; Nishioka Kusuki; Capanni Paolo; Conte Roberto; Ferrara Giovanni Battista
AUTHOR ADDRESS: Servizio di Immunogenetica, Centro di Biotecnologie Avanzate, Largo Rosanna Benzi, 10, 16132, Genova, Italy**Italy
JOURNAL: Transfusion (Bethesda) 41 (4): p462-469 April, 2001 2001
MEDIUM: print
ISSN: 0041-1132
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

6/3/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

15617946 BIOSIS NO.: 200000336259
Alloantigen-driven T cell death mediated by Fas ligand and tumor necrosis factor-alpha is not essential for the induction of allograft acceptance
AUTHOR: Wagener Maylene E; Konieczny Bogumila T; Dai Zhenhua; Ring Guido H; Lakkis Fadi G (Reprint)
AUTHOR ADDRESS: VAMC-151N, 1670 Clairmont Road, Atlanta, GA, 30033, USA** USA
JOURNAL: Transplantation (Baltimore) 69 (11): p2428-2432 June 15, 2000 2000
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

6/3/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

15509887 BIOSIS NO.: 200000228200
Pancreatic islet xenograft tolerance after short-term costimulation blockade is associated with increased CD4+ T cell apoptosis but not immune deviation
AUTHOR: Lehnert Anne M; Yi Shounan; Burgess Jane S; O'Connell Philip J (Reprint)
AUTHOR ADDRESS: National Pancreas Transplant Unit, Westmead Hospital, Westmead, NSW, 2145, Austria**Austria
JOURNAL: Transplantation (Baltimore) 69 (6): p1176-1185 March 27, 2000 2000
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

6/3/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13453821 BIOSIS NO.: 199699087881
CTLA-4 engagement inhibits IL-2 accumulation and cell cycle progression upon activation of resting T cells
AUTHOR: Krummel Matthew F; Allison James P (Reprint)
AUTHOR ADDRESS: Cancer Res Lab., 447 Life Sci. Addition, Univ. Calfironia, Berkeley, CA 94720, USA**USA
JOURNAL: Journal of Experimental Medicine 183 (6): p2533-2540 1996 1996
ISSN: 0022-1007
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

6/3/11 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

14212226 EMBASE No: 2006610400
The Role of Foxp3SUP+ Regulatory T Cells in Liver Transplant Tolerance
Li W.; Carper K.; Zheng X.X.; Kuhr C.S.; Reyes J.D.; Liang Y.; Perkins D.L.; Thomson A.W.; Perkins J.D.
W. Li, Department of Surgery, Division of Transplantation, University of Washington Medical Center, Seattle, WA United States
AUTHOR EMAIL: weili8@u.washington.edu
Transplantation Proceedings (TRANSPLANT. PROC.) (United States) 2006, 38/10 (3205-3206)
CODEN: TRPPA ISSN: 0041-1345
PUBLISHER ITEM IDENTIFIER: S0041134506013224
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 6

6/3/12 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

12603886 EMBASE No: 2004189242
Spontaneous T cell apoptosis in feline immunodeficiency virus (FIV)-infected cats is inhibited by IL2 and anti-B7.1 antibodies
Bull M.E.; Vahlenkamp T.W.; Dow J.L.; Collisson E.W.; Winslow B.J.; Phadke A.P.; Tompkins M.B.; Tompkins W.A.F.
W.A.F. Tompkins, Immunology Program, College of Veterinary Medicine, North Carolina State University, 4700 Hillsborough St., Raleigh, NC 27606 United States
AUTHOR EMAIL: wayne tompkins@ncsu.edu
Veterinary Immunology and Immunopathology (VET. IMMUNOL. IMMUNOPATHOL.) (Netherlands) 2004, 99/1-2 (25-37)
CODEN: VIIMD ISSN: 0165-2427
PUBLISHER ITEM IDENTIFIER: S0165242704000339
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 74

6/3/13 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE

12523424 EMBASE No: 2004116450
B7SUP+CTLA4SUP+ T cells engage in T-T cell interactions that mediate apoptosis: A model for lentivirus-induced T cell depletion
Vahlenkamp T.W.; Bull M.E.; Dow J.L.; Collisson E.W.; Winslow B.J.; Phadke A.P.; Tompkins W.A.F.; Tompkins M.B.
T.W. Vahlenkamp, Immunology Program, North Carolina State University, Raleigh, NC 27606 United States
AUTHOR EMAIL: thomas vahlenkamp@ncsu.edu
Veterinary Immunology and Immunopathology (VET. IMMUNOL. IMMUNOPATHOL.) (Netherlands) 2004, 98/3-4 (203-214)
CODEN: VIIMD ISSN: 0165-2427
PUBLISHER ITEM IDENTIFIER: S0165242703002794
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 46

6/3/14 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

10662377 EMBASE No: 2000145225
Pancreatic islet xenograft tolerance after short-term costimulation blockade is associated with increased CD4sup + T cell apoptosis but not immune deviation
Lehnert A.M.; Yi S.; Burgess J.S.; O'Connell P.J.
Dr. P.J. O'Connell, National Pancreas Transplant Unit, Westmead Hospital, Westmead, NSW 2145 Australia
Transplantation (TRANSPLANTATION) (United States) 27 MAR 2000, 69/6 (1176-1185)
CODEN: TRPLA ISSN: 0041-1337
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 48

6/3/15 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

10512730 EMBASE No: 1999423839
New immunosuppressive agents in renal transplantation
NUOVI AGENTI IMMUNOSOPPRESSORI NEL TRAPIANTO
Ponticelli C.; Montagnino G.
Prof. C. Ponticelli, Divisione di Nefrologia e Dialisi, Ospedale Maggiore IRCCS, Via Commenda 15, 20122 Milano Italy
Giornale Italiano di Nefrologia (G. ITAL. NEFROL.) (Italy) 1999, 16/2 (180-185)
CODEN: GINEE ISSN: 0393-5590
DOCUMENT TYPE: Journal; Article
LANGUAGE: ITALIAN SUMMARY LANGUAGE: ENGLISH; ITALIAN
NUMBER OF REFERENCES: 60

6/3/16 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14792018 PMID: 15010229
B7+CTLA4+ T cells engage in T-T cell interactions that mediate apoptosis: a model for lentivirus-induced T cell depletion.

Vahlenkamp Thomas W; Bull Marta E; Dow Janet L; Collisson Ellen W; Winslow Barbara J; Phadke Anagha P; Tompkins Wayne A F; Tompkins Mary B
Immunology Program, North Carolina State University, Raleigh, NC 27606, USA. thomas vahlenkamp@ncsu.edu
Veterinary immunology and immunopathology (Netherlands) Apr 2004, 98 (3-4) p203-14, ISSN 0165-2427--Print Journal Code: 8002006
Contract/Grant No.: AI38177; AI; NIAID; AI43858; AI; NIAID
Publishing Model Print
Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

6/3/17 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

140355753 CA: 140(22)355753t JOURNAL
Expression of CTLA-4 in nonhuman primate lymphocytes and its use as a potential target for specific immunotoxin-mediated apoptosis: results of in vitro studies
AUTHOR(S): Palmisano, G. L.; Tazzari, P. L.; Cozzi, E.; Bolognesi, A.; Polito, L.; Seveso, M.; Ancona, E.; Ricci, F.; Conte, R.; Stirpe, F.; Ferrara, G. B.; Pistillo, M. P.
LOCATION: Department of Oncology, Biology and Genetics, University of Genova, Genoa, Italy
JOURNAL: Clin. Exp. Immunol. (Clinical and Experimental Immunology)
DATE: 2004 VOLUME: 135 NUMBER: 2 PAGES: 259-266 CODEN: CEXIAL ISSN: 0009-9104 LANGUAGE: English PUBLISHER: Blackwell Publishing Ltd.

6/3/18 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

139394620 CA: 139(26)394620w JOURNAL
Study on the blocking effect of anti-CTLA-4 monoclonal antibody on the immunosuppression of tumor
AUTHOR(S): Luo, Liqiong; Lu, Xingyan; Lin, Yuexia; Hu, Licai; Wu, Tao
LOCATION: Institute of Biopharmaceuticals, Guangdong Pharmaceutical College, Canton, Peop. Rep. China, 510224
JOURNAL: Guangdong Yaoxueyuan Xuebao (Guangdong Yaoxueyuan Xuebao)
DATE: 2003 VOLUME: 19 NUMBER: 1 PAGES: 51-52 CODEN: GYXUF8
LANGUAGE: Chinese PUBLISHER: Guangdong Yaoxueyuan

6/3/19 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

138088613 CA: 138(7)88613d JOURNAL
CTLA-4 is not restricted to the lymphoid cell lineage and can function as a target molecule for apoptosis induction of leukemic cells
AUTHOR(S): Pistillo, Maria Pia; Tazzari, Pier Luigi; Palmisano, Giulio Lelio; Pierri, Ivana; Bolognesi, Andrea; Ferlito, Francesca; Capanni, Paolo ; Polito, Letizia; Ratta, Marina; Pileri, Stefano; Piccioli, Milena; Basso, Gluseppe; Rissotto, Laura; Conte, Roberto; Gobbi, Marco; Stirpe, Fiorenzo; Ferrara, Giovanni Battista
LOCATION: Laboratory of Immunogenetics and Laboratory of Molecular Morphogenesis, Advanced Biotechnology Center, National Cancer Research Institute, 16132, Genoa, Italy
JOURNAL: Blood (Blood) DATE: 2003 VOLUME: 101 NUMBER: 1 PAGES: 202-209 CODEN: BLOOAW ISSN: 0006-4971 LANGUAGE: English PUBLISHER:

American Society of Hematology

6/3/20 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

138023665 CA: 138(3)23665c PATENT
Use of human anti-CTLA-4 antibodies for treatment of cancer
INVENTOR(AUTHOR): Hanson, Douglas Charles; Mueller, Eileen Elliott
LOCATION: USA
ASSIGNEE: Pfizer Products Inc.
PATENT: European Pat. Appl. ; EP 1262193 A1 DATE: 20021204
APPLICATION: EP 2002253652 (20020523) *US PV293042 (20010523)
PAGES: 76 pp. CODEN: EPXXDW LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: A61K-039/395A; A61P-035/00B; C07K-016/28
DESIGNATED COUNTRIES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE; MC; PT; IE; SI; LT; LV; FI; RO; MK; CY; AL; TR

6/3/21 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

136165714 CA: 136(11)165714a JOURNAL
Costimulation blockade promotes the apoptotic death of graft-infiltrating T cells and prolongs survival of hepatic allografts from FLT3L-treated donors
AUTHOR(S): Li, Wei; Lu, Lina; Wang, Zhiliang; Wang, Lianfu; Fung, John J. ; Thomson, Angus W.; Qian, Shiguang
LOCATION: Thomas E. Starzl Transplantation Institute and Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, 15213, USA
JOURNAL: Transplantation DATE: 2001 VOLUME: 72 NUMBER: 8 PAGES: 1423-1432 CODEN: TRPLAU ISSN: 0041-1337 LANGUAGE: English PUBLISHER: Lippincott Williams & Wilkins

6/3/22 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

136048180 CA: 136(4)48180n JOURNAL
Immunotoxins containing recombinant anti-CTLA-4 single-chain fragment variable antibodies and saporin: in vitro results and in vivo effects in an acute rejection model
AUTHOR(S): Tazzari, Pier-Luigi; Polito, Letizia; Bolognesi, Andrea; Pistillo, Maria-Pia; Capanni, Paolo; Palmisano, Giulio Lelio; Lemoli, Roberto M.; Curti, Antonio; Biancone, Luigi; Camussi, Giovanni; Conte, Roberto; Ferrara, Giovanni B.; Stirpe, Fiorenzo
LOCATION: Service of Transfusion Medicine, S. Orsola-Malpighi Hospital, Bologna, Italy
JOURNAL: J. Immunol. DATE: 2001 VOLUME: 167 NUMBER: 8 PAGES: 4222-4229 CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists

6/3/23 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

136036352 CA: 136(3)36352g PATENT
Identification of unique binding interactions between certain antibodies

and the human B7.1 and B7.2 costimulatory antigens
INVENTOR(AUTHOR): Anderson, Darrell R.; Hanna, Nabil; Brams, Peter
LOCATION: USA
ASSIGNEE: Idec Pharmaceuticals Corporation
PATENT: PCT International ; WO 200189567 A1 DATE: 20011129
APPLICATION: WO 2001US16364 (20010522) *US 576424 (20000522)
PAGES: 89 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: A61K-039/395A; C07K-016/28B
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

6/3/24 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

124229989 CA: 124(17)229989f PATENT
Ligands for induction of antigen specific apoptosis in T cells
INVENTOR(AUTHOR): Gribben, John G.; Freeman, Gordon J.; Nadler, Lee M.; Rennert, Paul; Jellis, Cindy L.; Greenfield, Edward; Gray, Gary S.
LOCATION: USA
ASSIGNEE: Repligen Corp.; Dana Farber Cancer Institute
PATENT: PCT International ; WO 9533770 A1 DATE: 951214
APPLICATION: WO 95US6726 (950602) *US 253783 (940603)
PAGES: 86 pp. CODEN: PIXXD2 LANGUAGE: English
PATENT CLASSIFICATIONS:
CLASS: C07K-014/705A; C07K-016/28B; A61K-039/395B; A61K-038/17B
DESIGNATED COUNTRIES: AU; CA; JP DESIGNATED REGIONAL: AT; BE; CH; DE; DK ; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE
?